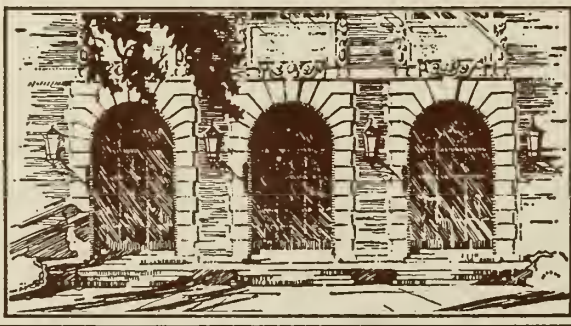


LIBRARY OF THE
UNIVERSITY OF ILLINOIS
AT URBANA-CHAMPAIGN

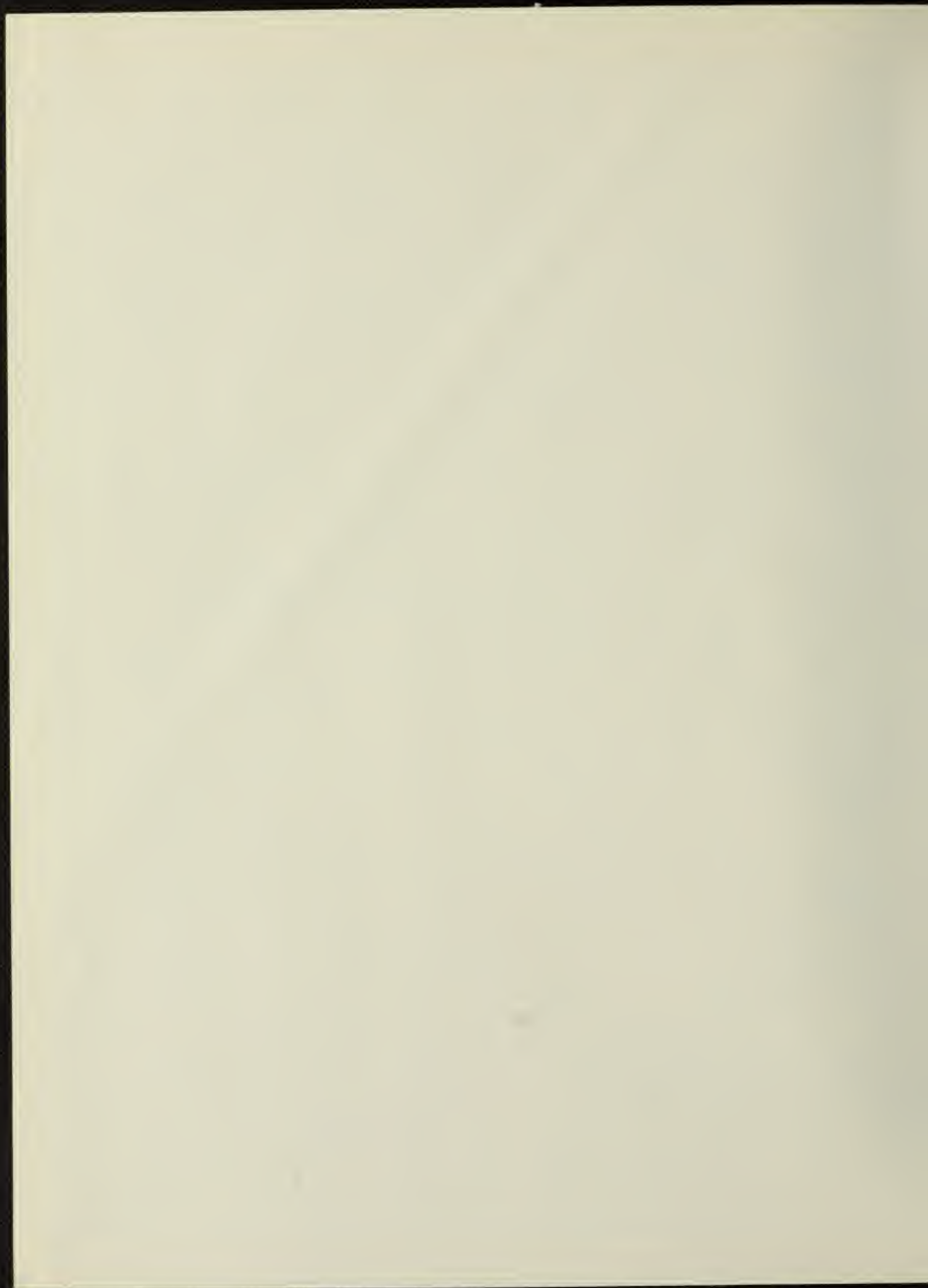
616.99405

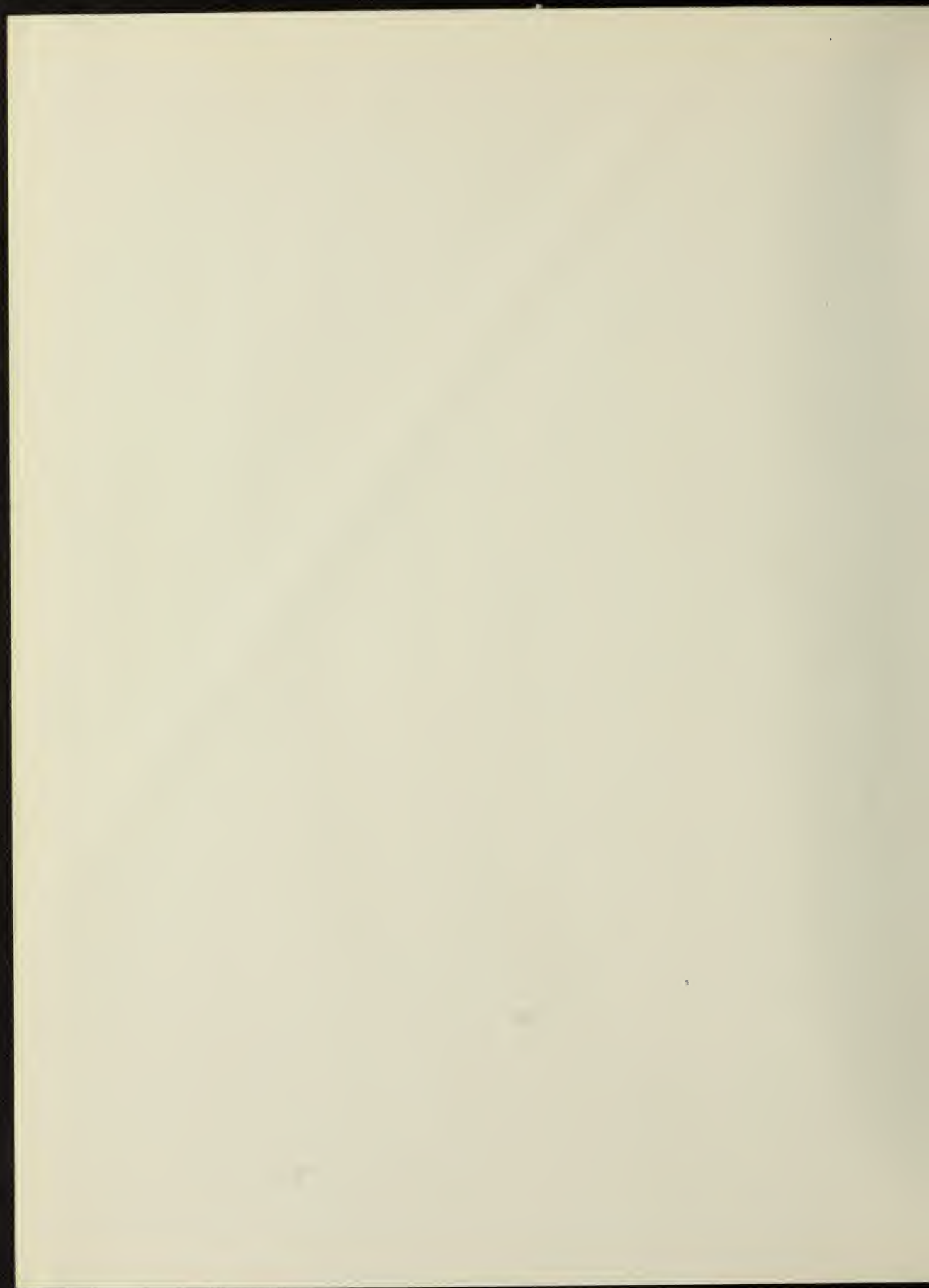
CAR

v. 9



~~VETERINARY MEDICINE~~





CARCINOGENESIS ABSTRACTS

A monthly publication of the

National Cancer Institute

Editor

Robert Love, M.D.

Jefferson Medical College, Philadelphia

Associate Editor

George P. Studzinski, M.D.

Jefferson Medical College, Philadelphia

NCI Staff Consultants

Howard R. Rosenberg, M.S.

Sidney Siegel, Ph.D.

Elizabeth Weisburger, Ph.D.

Literature Selected, Abstracted, and Indexed
by

The Franklin Institute Research Laboratories
Science Information Services
Biomedical Section

M. H. Fukami, Ph.D., Technical Editor

Contract Number NIH-71-2073

Public Health Service, USDHEW

THE HISTORY OF THE

OF THE

OF THE

OF THE

OF THE

OF THE

OF THE

OF THE

OF THE

OF THE

OF THE

OF THE

OF THE

616,99405
CAR
v.9

Uet Met

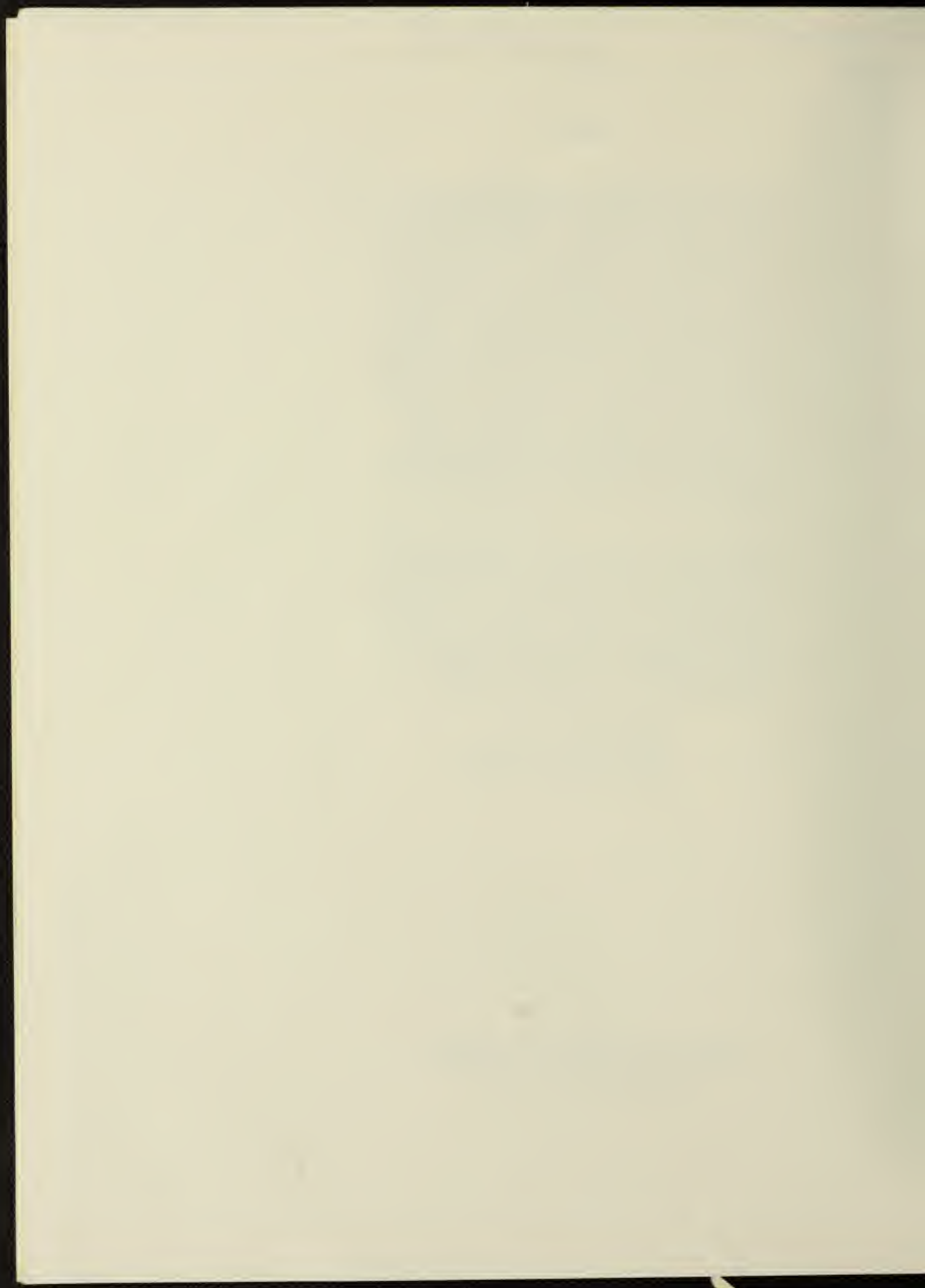
PREFACE

Carcinogenesis Abstracts is a publication of the National Cancer Institute. The journal serves as a vehicle through which current documentation of carcinogenesis research highlights are compiled, condensed, and disseminated on a regular basis. It represents an integral part of the Institute's program of fostering and supporting coordinated research into cancer etiology. Issues of *Carcinogenesis Abstracts* normally contain two-hundred abstracts and twenty citations (unaccompanied by corresponding abstracts). Abstracts and citations refer to the current scientific literature that describes the most significant carcinogenesis research carried on at the National Cancer Institute, other governmental agencies, and private institutions. *Carcinogenesis Abstracts* is intended to be a highly useful current awareness tool for scientists engaged in carcinogenesis research or related areas. The great number and diversity of publications relevant to carcinogenesis make imperative the availability of this service to investigators whose work requires that they keep abreast with current developments in the field.

Carcinogenesis Abstracts is normally published monthly. Volume IX covers the scientific literature published from July 1970 through June 1971. A cumulative subject and author index for Volume IX will be published shortly after the final regular issue. This journal is available free of charge to libraries and to individuals who have a professional interest in carcinogenesis. Requests for *Carcinogenesis Abstracts* from qualified individuals should include statements of their relationship to carcinogenesis research. All correspondence should be addressed as follows:

Carcinogenesis Abstracts
Etiology Area
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20014

Use of Funds for Printing this publication
approved by the Director of the Bureau of
the Budget on July 25, 1967.



NOTE

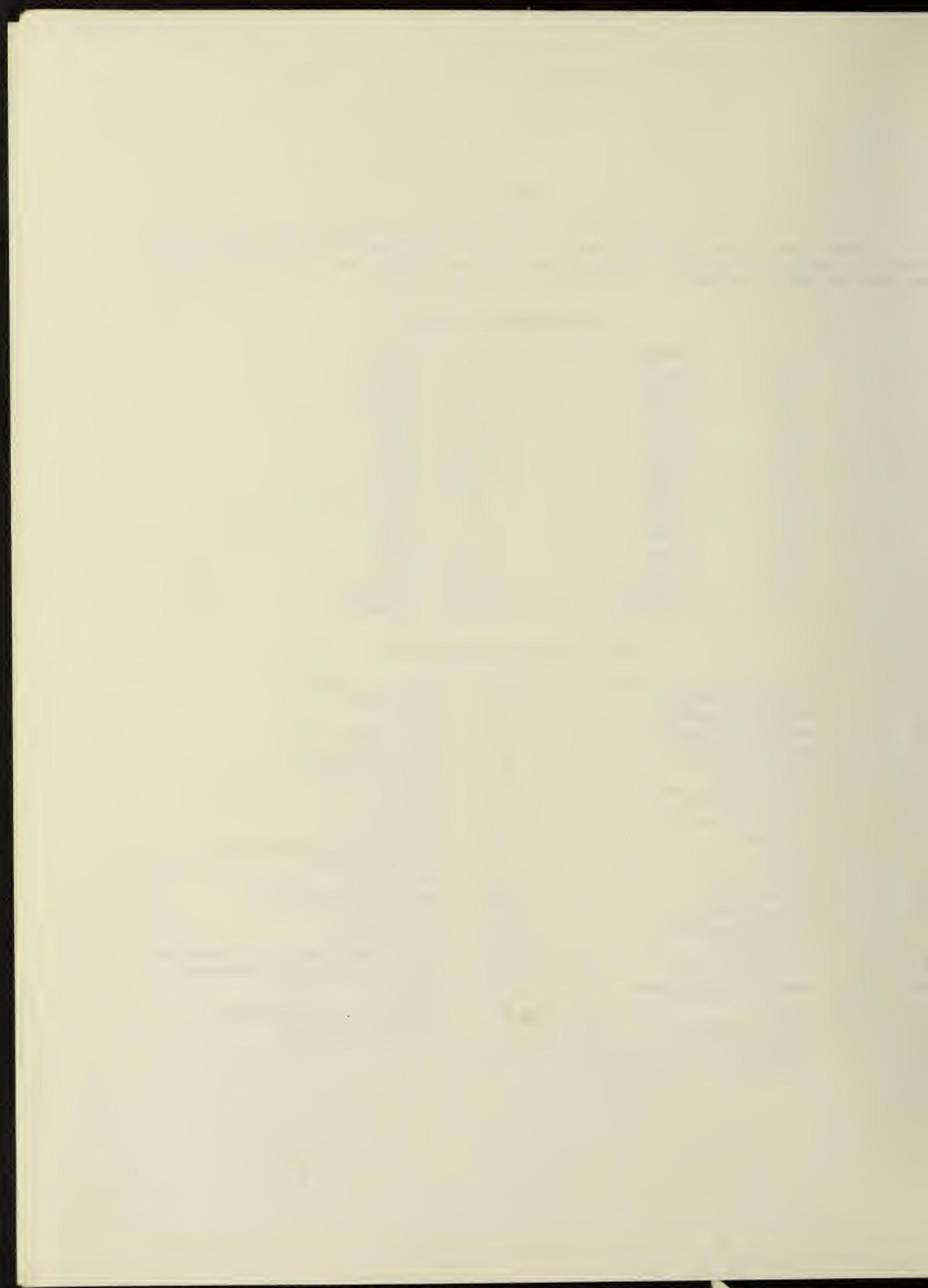
Journal names are abbreviated according to the list of abbreviations used by *Index Medicus*. For journals not covered by *Index Medicus*, the abbreviations (with some modifications) found in *World Medical Periodicals*, 3rd Edition, are used.

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	It.	Italian
Ar.	Arabic	Jap.	Japanese
Bul.	Bulgarian	Kor.	Korean
Ch.	Chinese	Latv.	Latvian
Cz.	Czech	Lith.	Lithuanian
Dan.	Danish	Nor.	Norwegian
Dut.	Dutch	Pol.	Polish
E.	English	Por.	Portuguese
Eston.	Estonian	Rum.	Rumanian
Fin.	Finnish	Rus.	Russian
Fl.	Flemish	Ser.	Serbo-Croatian
Fr.	French	Sl.	Slovak
Ger.	German	Sp.	Spanish
Gr.	Greek	Sw.	Swedish
Heb.	Hebrew	Th.	Thai
Hun.	Hungarian	Turk.	Turkish
Ic.	Icelandic	Uk.	Ukrainian
In.	Indonesian	Viet.	Vietnamese

ABBREVIATIONS USED IN ABSTRACTS

ACTH	adrenocorticotrophic hormone	mC, μ C	milli-, microcurie(s)
ADP	adenosine diphosphate	mg	milligram(s)
AMP	adenosine monophosphate	min	minute(s)
ATP	adenosine triphosphate	ml	milliliter(s)
BSP	sulfobromophthalein	mm	millimeter(s)
C	degrees centigrade	MTD	maximum tolerated dose
cm	centimeter(s)	ng	nanogram (10^{-9})
CNS	central nervous system	pg	picogram (10^{-12})
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	ppm	parts per million
e.g.	for example	r	Roentgen
g	gram(s)	RBC	red blood cells (erythrocytes), red blood count
μ g	microgram(s)	resp.	respectively
hr	hour(s)	Rev.	review (only in citations)
i.m.	intramuscular	RNA	ribonucleic acid
i.p.	intraperitoneal	s.c.	subcutaneous
IU	international unit(s)	sec	second(s)
i.v.	intravenous	SGOT	serum glutamic-oxalacetic transaminase
kg	kilogram(s)	SGPT	serum glutamic-pyruvic transaminase
LD ₅₀	median lethal dose(s)	U	unit(s)
LDH	lactic acid dehydrogenase	UV	ultraviolet
m	meter(s)	WBC	white blood cells (leukocytes), white blood count
M	molar	yr	year(s)
mEq	milliequivalent(s)		
mM	millimolar		
μ M	micromolar		

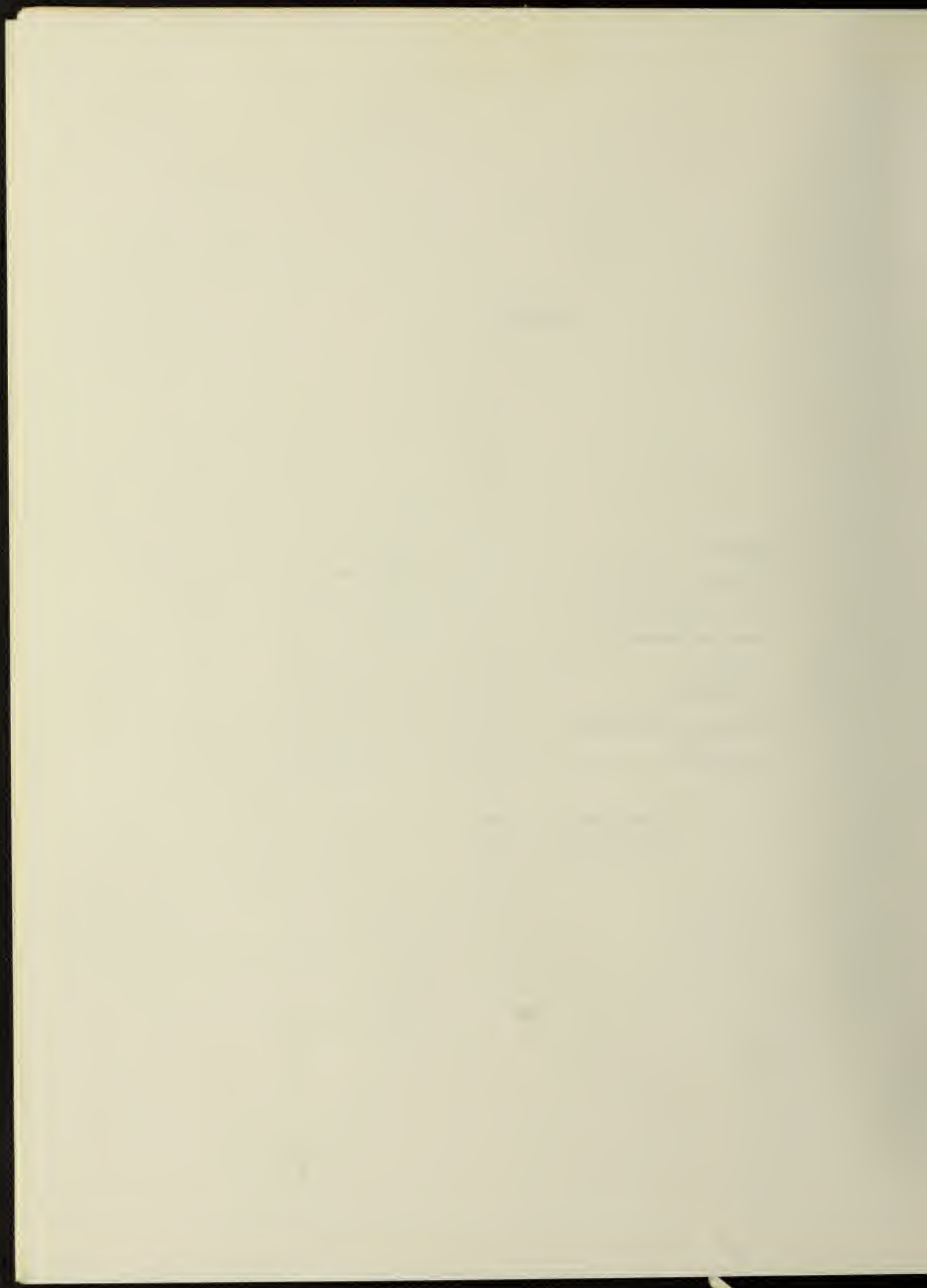


CONTENTS

	Page
REVIEW.....	1, 67, 173, 277, 379, 471
CHEMICAL CARCINOGENESIS.....	5, 76, 183, 282, 386, 476
PHYSICAL CARCINOGENESIS.....	26, 104, 210, 303, 403, 496
VIRAL CARCINOGENESIS.....	29, 111, 217, 309, 409, 501
IMMUNOLOGY.....	46, 143, 242, 334, 431, 523
PATHOGENESIS.....	50, 152, 249, 350, 444, 539
EPIDEMIOLOGY AND BIOMETRY.....	54, 155, 254, 354, 446, 542
MISCELLANEOUS.....	61, 159, 261, 361, 450, 547

AUTHOR INDEX.....565

SUBJECT INDEX.....615



99405
R

Vet. Med.

JULY-AUGUST 1970

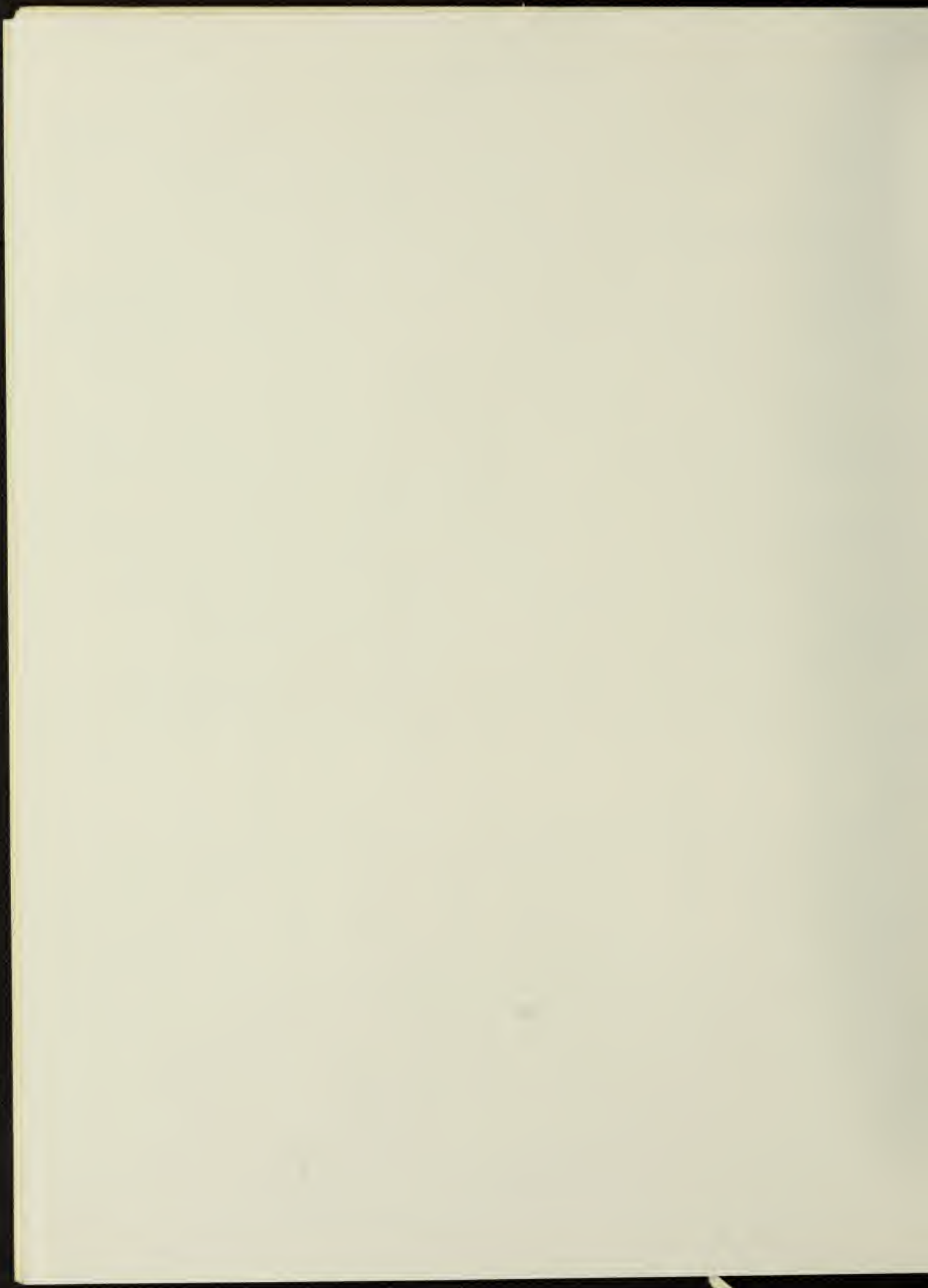
Abstract Nos. 1-343

**Vol. 9
Nos. 1-2**

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health



CARCINOGENESIS ABSTRACTS

A monthly publication of the

National Cancer Institute

Editor

Robert Love, M.D.
Jefferson Medical College, Philadelphia

Associate Editor

George P. Studzinski, M.D.
Jefferson Medical College, Philadelphia

NCI Staff Consultants

Elizabeth Weisberger, Ph.D.

Louis P. Greenberg, M.S.

Howard R. Rosenberg, M.S.

Literature Selected, Abstracted, and Indexed
by

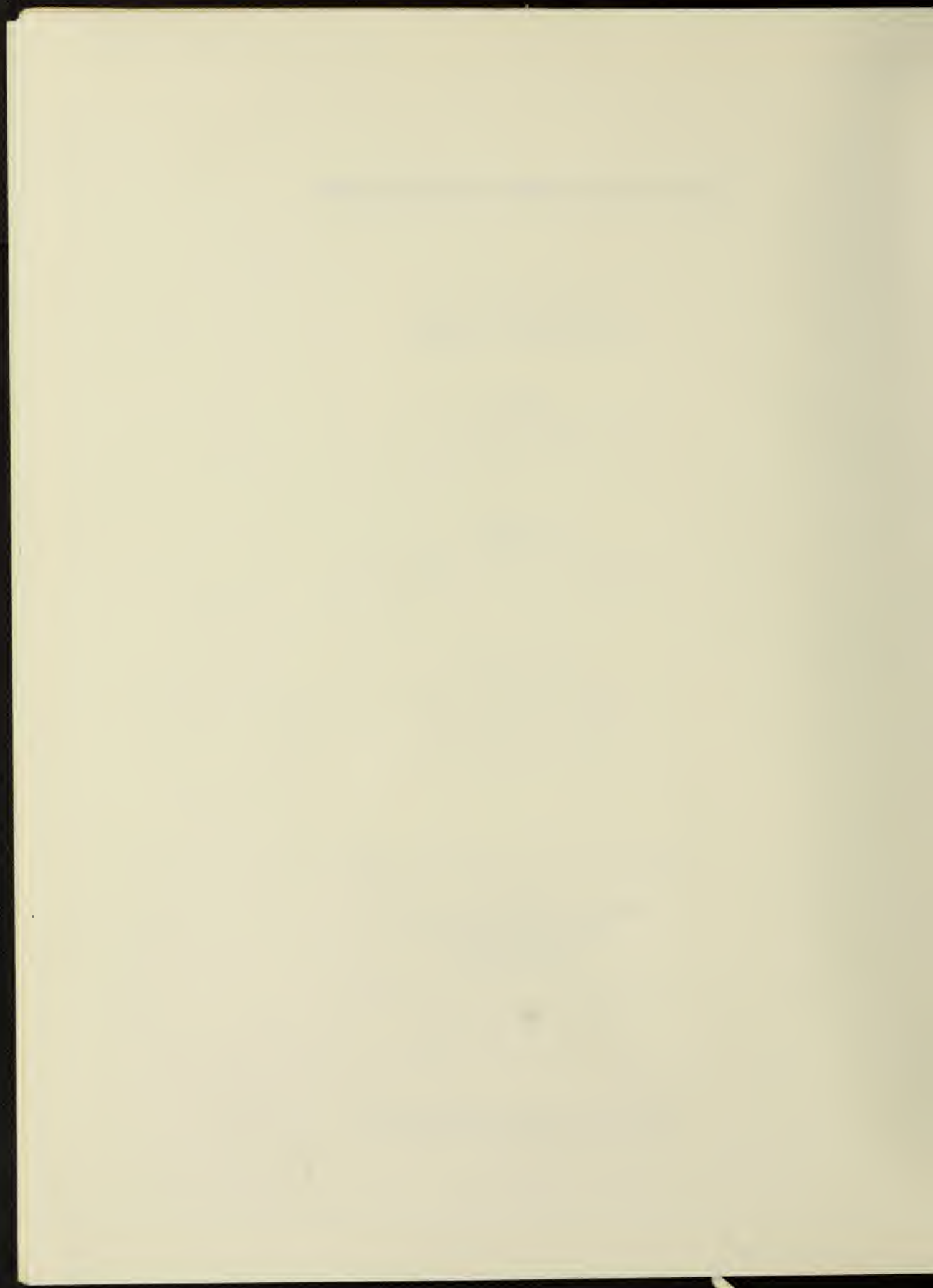
The Franklin Institute Research Laboratories
Science Information Services
Biomedical Section

M. H. Fukami, Ph.D., Technical Editor

Contract Number NIH-71-2073

Public Health Service, USDHEW

Use of Funds for Printing this publication
approved by the Director of the Bureau of
the Budget on July 25, 1967.

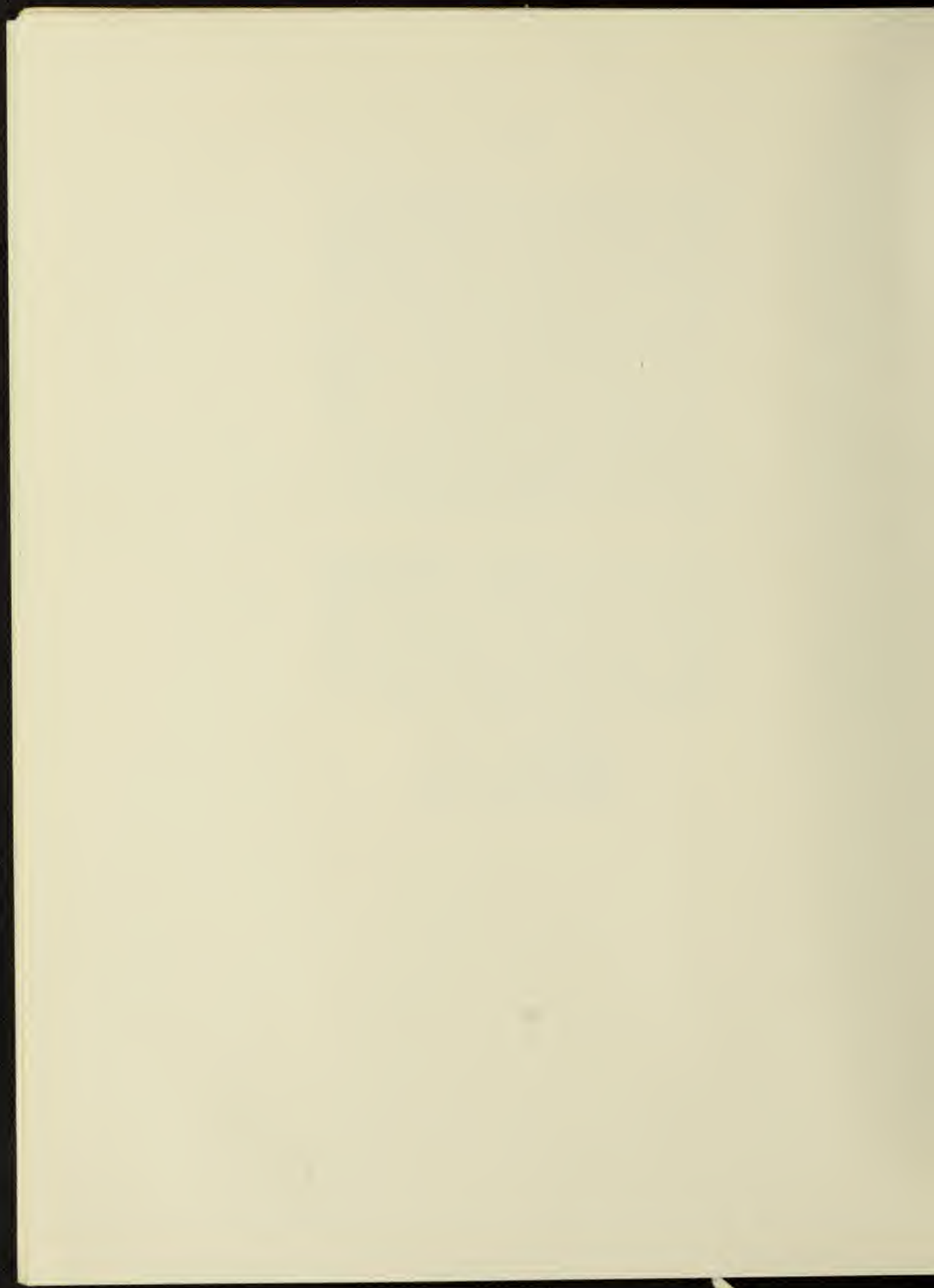


PREFACE

Carcinogenesis Abstracts is a publication of the National Cancer Institute. The journal serves as a vehicle through which current documentation of carcinogenesis research highlights are compiled, condensed, and disseminated on a regular basis. It represents an integral part of the Institute's program of fostering and supporting coordinated research into cancer etiology. Issues of *Carcinogenesis Abstracts* normally contain two-hundred abstracts and twenty citations (unaccompanied by corresponding abstracts). Abstracts and citations refer to the current scientific literature that describes the most significant carcinogenesis research carried on at the National Cancer Institute, other governmental agencies, and private institutions. *Carcinogenesis Abstracts* is intended to be a highly useful current awareness tool for scientists engaged in carcinogenesis research or related areas. The great number and diversity of publications relevant to carcinogenesis make imperative the availability of this service to investigators whose work requires that they keep abreast with current developments in the field.

Carcinogenesis Abstracts is normally published monthly. Volume IX covers the scientific literature published from July 1970 through June 1971. A cumulative subject and author index for Volume IX will be published shortly after the final regular issue. This journal is available free of charge to libraries and to individuals who have a professional interest in carcinogenesis. Requests for *Carcinogenesis Abstracts* from qualified individuals should include statements of their relationship to carcinogenesis research. All correspondence should be addressed as follows:

Carcinogenesis Abstracts
Etiology Area
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20014



NOTE

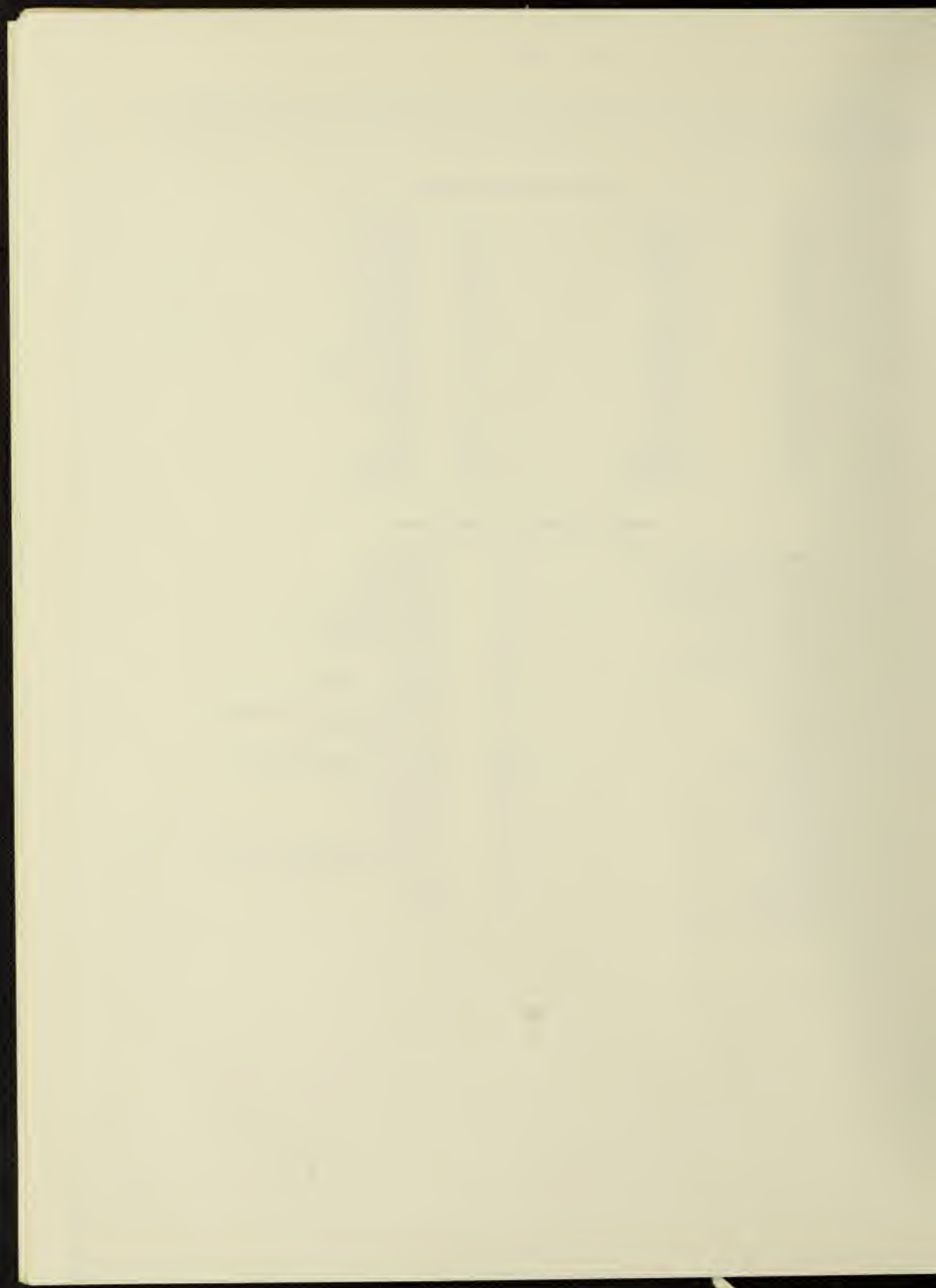
Journal names are abbreviated according to the list of abbreviations used by *Index Medicus*. For journals not covered by *Index Medicus*, the abbreviations (with some modifications) found in *World Medical Periodicals*, 3rd Edition, are used.

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	It.	Italian
Ar.	Arabic	Jap.	Japanese
Bul.	Bulgarian	Kor.	Korean
Ch.	Chinese	Latv.	Latvian
Cz.	Czech	Lith.	Lithuanian
Dan.	Danish	Nor.	Norwegian
Dut.	Dutch	Pol.	Polish
E.	English	Por.	Portuguese
Eston.	Estonian	Rum.	Rumanian
Fin.	Finnish	Rus.	Russian
Fl.	Flemish	Ser.	Serbo-Croatian
Fr.	French	Sl.	Slovak
Ger.	German	Sp.	Spanish
Gr.	Greek	Sw.	Swedish
Heb.	Hebrew	Th.	Thai
Hun.	Hungarian	Turk.	Turkish
Ic.	Icelandic	Uk.	Ukrainian
In.	Indonesian	Viet.	Vietnamese

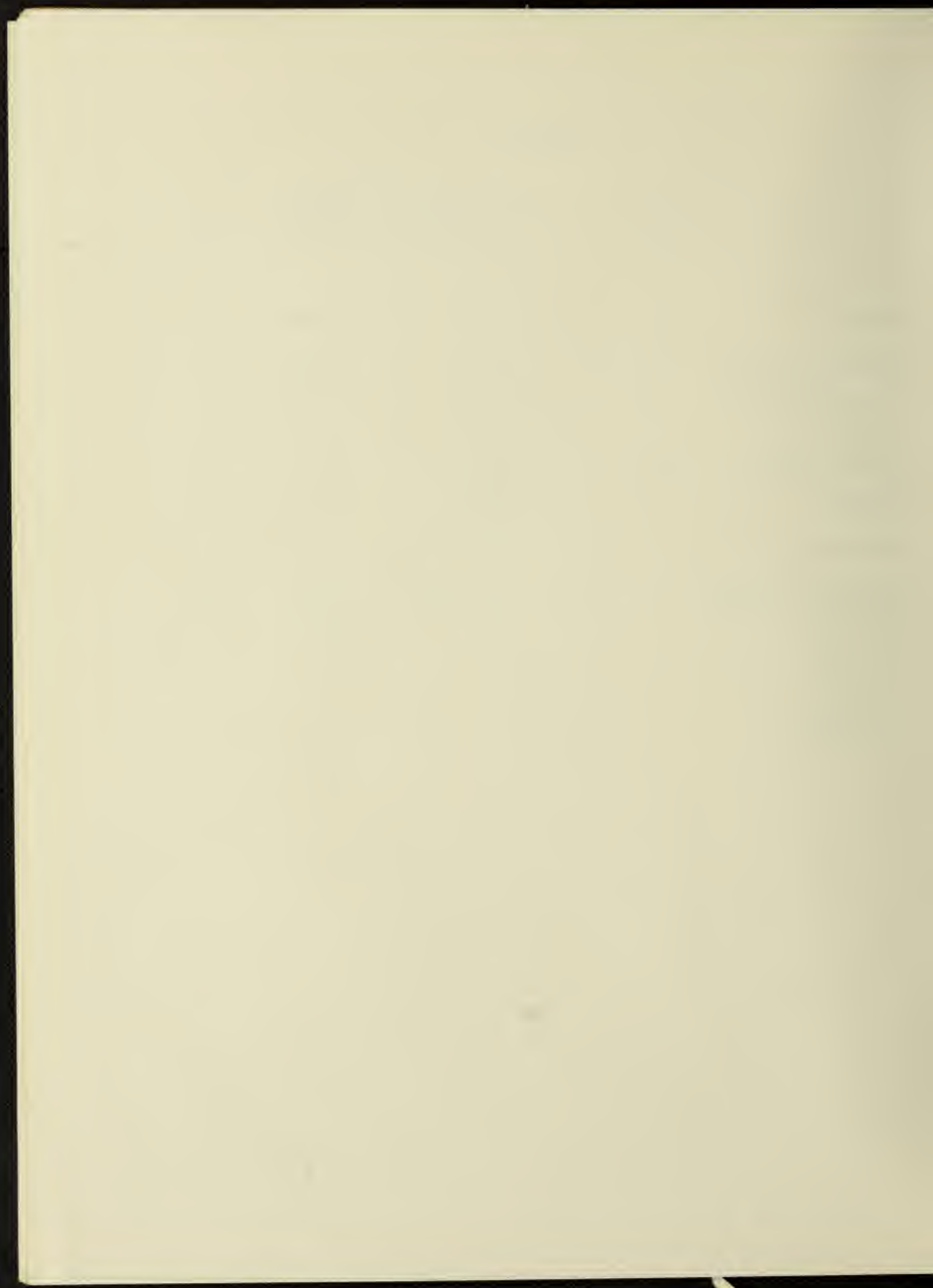
ABBREVIATIONS USED IN ABSTRACTS

ACTH	adrenocorticotrophic hormone	mg	milligram(s)
ADP	adenosine diphosphate	min	minute(s)
AMP	adenosine monophosphate	ml	milliliter(s)
ATP	adenosine triphosphate	mm	millimeter(s)
C	degrees centigrade	MTD	maximum tolerated dose
cm	centimeter(s)	ng	nanogram (10^{-9})
CNS	central nervous system	pg	picogram (10^{-12})
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	ppm	parts per million
e.g.	for example	r	Roentgen
g	gram(s)	RBC	red blood cells (erythrocytes), red blood count
µg	microgram(s)	resp.	respectively
hr	hour(s)	Rev.	review (only in citations)
i.m.	intramuscular	RNA	ribonucleic acid
i.p.	intraperitoneal	s.c.	subcutaneous
IU	international unit(s)	sec	second(s)
i.v.	intravenous	U	unit(s)
kg	kilogram(s)	UV	ultraviolet
LD ₅₀	median lethal dose(s)	WBC	white blood cells (leukocytes), white blood count
m	meter(s)	wk	week
M	molar	wt	weight
mEq	milliequivalent(s)	yr	year(s)
mM	millimolar		
µM	micromolar		
mC, µC	milli-,microcurie(s)		



CONTENTS

	Cross Reference Abbreviations	Abstracts, Citations	Page
REVIEW.	(Rev).	0001-0021	1
CHEMICAL CARCINOGENESIS	(Chem)	0022-0122	5
PHYSICAL CARCINOGENESIS	(Phys)	0123-0140	26
VIRAL CARCINOGENESIS.	(Viral).	0141-0221	29
IMMUNOLOGY.	(Immun).	0222-0243	46
PATHOGENESIS.	(Path)	0244-0263	50
EPIDEMIOLOGY AND BIOMETRY	(Epid-Biom).	0264-0303	54
MISCELLANEOUS	(Misc)	0304-0343	61
AUTHOR INDEX			i
SUBJECT INDEX			x



- 0001 MALIGNANCY FROM RADIUM. (E.) Loutit, J. F. (Med. Res. Counc., Harwell, Didcot, Berkshire, England). *Brit J Cancer* 24(2):195-207, 1970.

A review of the literature of the carcinogenic efficacy of occupationally or therapeutically acquired radium indicates that osteosarcoma has been regarded as the chief limiting hazard of internally retained radium. Other malignancies associated with radium exposure are carcinoma of the mucosa in the cranial air passages, bone marrow dyscrasia and a "regenerative euopenic anemia" with features of atypical leukemia. Three cases of radium poisoning from England showed features compatible with aleukemic leukemia and malignant myelosclerosis, a finding which supports the thesis that malignant transformation in the lymphomyeloid complex should be added to the accepted malignancies of bone and cranial sinus epithelium as limiting hazards from retention of radium. (31 references)

- 0002 VARIABILITY, STRUCTURAL GLYCOPROTEINS AND CLASSIFICATION OF HERPES SIMPLEX VIRUSES. (E.) Roizman, B. (Dept. Microbiol., U. Chicago, Ill.), M. Keller, P. G. Spear, M. Terni, A. Nahamias and J. Dowdle. *Nature* 227(5264):1253-1254, 1970.

Although herpes simplex virus, which has been implicated in cancer of the cervix and lip, is usually divided into 2 types, those isolated from lesions on body parts other than the genitals and those isolated from genital lesions, these viruses do not fall naturally into 2 classes, but form a continuously varying spectrum. Type 2 variants of herpes simplex virus strains have given rise to type 1 strains, and virus strains intermediate between the two types have been described. The MP strain of the virus appears in neutralization tests to be intermediate between 2 prototypical strains from each of the 2 divisions. Furthermore, herpes simplex virus is very variable in the laboratory, giving rise to a wide spectrum of mutant strains. The basis of the high variability of the surface of the virus might be the nature of the envelope of the virus, which may be affected by glycosylating enzymes in the host from which the viruses are derived. In spite of their clinical and behavioral differences, and the differences in the buoyant densities of their DNAs, the genetic differences between type 1 and type 2 herpes simplex virus are minor and are breached by multiple mutations in the laboratory. (29 references)

- 0003 CANCER VIRUSES IN PRIMATES. (E.) Kinard, R. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *Science* 169(3948):828-831, 1970.

Four projects in the Special Virus Cancer Program are described in which breeding colonies of primates are developed for the purpose of providing newborns to be inoculated with a variety of known viruses or malignant cells presumed to contain viruses. Newborn primates at the Bioentics Research Laboratories, Kensington, Maryland are inoculated with the following agents: adenovirus 12, simian virus 40, echovirus 9, reovirus 1, reovirus from Burkitt's lymphoma, Rous sarcoma vi-

rus, Moloney sarcoma virus, rubella virus, herpes genitalis virus, herpes-type particles in chimpanzee leukocyte culture; tissues and cells from patients with myelogenous leukemia (acute and chronic), lymphocytic leukemia (acute and chronic), Hodgkin's disease, Burkitt's lymphoma, polycythemia, rhabdomyosarcoma, epidermoid carcinoma, warts, infectious mononucleosis, and myelogenous leukemia. Inocula studied at the Baylor College of Medicine, Houston, Texas, include: fresh plasma or bone marrow cells from children with acute leukemia, human wart suspension; lymphoblastoid cell cultures from patients with leukemia, Burkitt's lymphoma, or infectious mononucleosis; adenoviruses 2, 7, and 12; reoviruses 1 and 3; echovirus 9; simian adenovirus 7, 3 strains of rubella virus; cytomegalovirus; and herpes simplex virus. In this project, the following carcinogens are also studied: X-irradiation, Imuran, prednisone, urethan, benzpyrene. At Presbyterian-St. Luke's Hospital in Chicago, inocula of the following origins are used: Bryan strain Rous sarcoma virus, DiGuglielmo's syndrome (erythroleukemia), human papilloma, Burkitt lymphoma (Epstein-Barr virus), Kaposi sarcoma, and cat leukemia. This project has succeeded in inducing fatal metastasizing sarcomas in marmosets by inoculation with the Schmidt-Ruppin strain of Rous sarcoma virus. The fourth project, at the Institute for Comparative Biology of the Zoological Society of San Diego, California, is concerned with evaluation of the reproductive potential in captivity of several species of small primates. (13 references)

- 0004 EPSTEIN-BARR VIRUS, INFECTIOUS MONONUCLEOSIS AND BURKITT'S LYMPHOMA. (Ger.) Waubke, R. (Med. Clin. Polyclin. U. Giessen, Germany). *Deutsch Med Wschr* 95(30):1572-1578, 1970.

Experimental investigations with Epstein-Barr virus (EBV) and its relation to infectious mononucleosis, Burkitt's lymphoma and other malignant tumors are reviewed. EBV induces a latent or not yet clinically correlated viral infection in man usually during childhood. The incidence of this infection is about 2000 times higher than that of infectious mononucleosis. EBV may induce infectious mononucleosis in adults lacking EBV-antibodies, subsequent organ infiltration and leukemia may occur. Infectious mononucleosis is possibly an immune response to an oncogenic viral infection. (69 references)

- 0005 BURKITT LYMPHOMA AND MALARIA. (E.) Anonymous. *Lancet* 2(7667):300-301, 1970.

The epidemiological evidence incriminating malaria as a contributory factor in the etiology of Burkitt lymphoma is reviewed. Burkitt lymphoma is concentrated in the 2 areas of the world (tropical Africa and New Guinea) where malaria is holoendemic; anomalies in the distribution of Burkitt lymphoma may be linked with local control of malaria. Epstein-Barr virus has been identified in Burkitt tumor cells, but the nature of the interaction between virus, malarial parasite, and lymphoid tissues remains obscure. The simplest view is that lymphoid tissues which are subjected to persistent stimuli and stress by the parasites are somehow rendered more suscep-

tible to neoplastic transformation in the presence of Epstein-Barr virus. The reticuloendothelial system is probably involved, but evidence of anti-malarial immunity and of enhanced non-specific activity in this system is not forthcoming. Incompatible with the theory of the essential involvement of the reticuloendothelial system is the fact that patients with Burkitt lymphoma have normal or low levels of serum-immunoglobulins, usually accurate indices of immunological stress and response. (19 references)

- 0006 BURKITT'S LYMPHOMA AND MALARIA. (E.)
Burkitt, D. P. (Med. Res. Council External Staff, London, England) and G. W. Kafuko. *Int J Cancer* 6(1):1-9, 1970.

The evidence for a relationship between Burkitt's lymphoma and malaria is reviewed. Burkitt's lymphoma is known to be endemic only in areas where malaria is still holoendemic or hyperendemic. Areas where intensive malaria eradication campaigns have been undertaken are nearly tumor free, and in areas where malaria control has been instituted only recently, a marked fall in incidence of Burkitt's lymphoma has been observed. The peak age-incidence of Burkitt's tumors corresponds to the period of highest malarial infestation. A lower incidence of sickle cell anemia and AS type hemoglobin which confers a relative immunity to malaria, is seen in patients suffering from Burkitt's lymphoma. Mice infected with chronic malaria and subsequently developing an immunity, showed an increased susceptibility to this tumor. The evidence suggests a causal relationship between malaria and Burkitt's lymphoma. (28 references)

- 0007 GLUCOSE METABOLISM IN TUMORS AND VARIOUS THEORIES ON CANCER BIOCHEMISTRY. (Ger.)
Gorlich, M. (Robert Rossle Clin., German Acad. Sci., Berlin). *Arch Geschwulstforsch* 35(3):261-277, 1970.

The role of glucose metabolism in tumors as related to carcinogenesis and specific tumor cell metabolism is reviewed. Warburg's hypothesis on aerobic glycolysis as a specific feature of tumor tissue metabolism and growth, Greenstein's convergency hypothesis (enzyme functions and gradual dedifferentiation), Miller & Miller's deletion hypothesis (azo dye carcinogenesis), Potter's catabolic deletion theory (enzyme protein breakdown), the feedback deletion theory (alterations in the regulation of transfer of genetic information), extra- and intracellular regulation defects of tumors and Hecker's information theory on cancerization (the initiation stage), are analyzed. It is concluded that the alterations in glucose metabolism should be considered as secondary events and not a primary cause in tumorigenesis. (84 references)

- 0008 CONTROL OF LYMPHOCYTE LEVEL IN THE BLOOD. (E.) Vincent, P. C. (Sydney Hosp., New South Wales, Australia) and F. W. Gunz. *Lancet* 2 (7668):342-344, 1970.

A model for control of lymphocyte proliferation involving a feedback mechanism is proposed. Detection of a recognition site on the surface of lymphocytes by the lymph node endothelium is suggested as a mechanism responsible for inhibition of proliferation. This recognition site could be identical or closely associated with the site(s) which react with phytohemagglutinin and other specific antigens to which the cell is committed. Cells in which the recognition site is either absent or blocked would not be detected by the lymph node endothelium, and proliferation would not be inhibited. The fundamental defect in chronic lymphocytic leukemia may be the loss of such a recognition site from the cell surface. (23 references)

- 0009 LYMPHOID STIMULATION AND LYMPHOID NEOPLASIA (E.) Anonymous. *Lancet* 2(7673):596-598, 1970.

The possible links between aberrant immune reactions and malignant lymphoma and leukemias are considered with particular reference to autoimmune processes. Hemolytic anemia, idiopathic thrombocytopenic purpura, Hashimoto's disease, rheumatoid arthritis, systemic lupus erythematosus and the Sjögren-Mikulicz syndrome are autoimmune conditions formerly thought to be exclusively symptomatic of the underlying malignancy, but now thought to be forerunners of the neoplastic process and perhaps intimately related to it. Continuous stimulation by self-antigen may evoke a sustained proliferative expansion of the forbidden clone of lymphoid cells, leading to neoplasia. Applicable examples of animal models are cited. (24 references)

- 0010 PHILADELPHIA CHROMOSOME IN LEUKEMIA. (E.) Anonymous. *Brit Med J* 3(5720):419, 1970.

The Philadelphia chromosome, which is accepted as a diagnostic sign of chronic myeloid leukemia, may not always be present in chronic myeloid leukemia, and it is occasionally found in patients presenting as cases of polycythemia. Because of the difference in treatments, the possibility of eosinophilic leukemia, a variant of chronic myeloid leukemia, should be considered in polycythemic patients who have a high white cell count at the time of presentation. Although there is evidence that hemopoietic cells other than those of the granulocyte series, specifically erythroblasts and megakaryocytes, show the Philadelphia chromosome condition, it is still thought that the Philadelphia chromosome abnormality is primarily associated with chronic myeloid leukemia not as its primary cause but as a secondary effect. (10 references)

- 0011 MEDICAL SYNDROMES ASSOCIATED WITH MALIGNANT TUMORS. (E.) Schottenfeld, D. (Mem. Sloan Kettering Cancer Ctr., New York, N. Y.). *CA* 20(1):35-43, 1970.

Twenty-two symptom complexes and metabolic aberrations which may be associated with cancer are listed, including dermatomyositis (associated with

lung, breast, and stomach cancer, and lymphoma); disseminated lupus erythematosus (associated with Hodgkin's disease and chronic lymphocytic leukemia); acute arthritic symptoms (associated with acute lymphatic leukemia in children); parenchymatous cerebellar degeneration (associated with lung and breast cancers); hypoglycemia and extra-pancreatic tumors (associated with fibrosarcoma and other mesodermal tumors); and polycythemia (associated with hepatoma and uterine fibroma). Tumors may be associated with disease of the connective tissue, neuromyopathies, and multifocal leukoencephalopathy by means of altered immune or auto-immune responses to organ-specific antigens which are elaborated by the malignancy. There is evidence that a tumor arising from non-endocrine tissue may synthesize peptides and proteins with hormonal activity, causing paradoxical hormonal effects. These effects may arise from the derepression or activation of latent coding functions in the DNA of tumor cells. (68 references)

- 0012 NONGONADAL NEOPLASIA IN TURNER'S SYNDROME. (E.) Wiertelcki, W. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), J. F. Fraumeni, Jr. and J. J. Mulvihill. *Cancer* 26(2):485-588, 1970.

The possibility that nongonadal neoplasia are associated with Turner's syndrome was investigated in a multihospital survey involving 289 patients. Of these patients 8 had nongonadal neoplasms (ganglioneuroma, carcinoid tumor, granular-cell myoblastoma, gastrointestinal carcinoma, leukemia, carcinoma of the thyroid); 1 patient had a hilus cell adenoma. A series of 20 patients with "male Turner's syndrome" revealed 2 patients with neurogenic tumors (pheochromocytoma and ganglioneuroma). The tendency to develop neurogenic tumors may be shared by syndromes with a Turner phenotype irrespective of a visible chromosomal defect. (29 references)

- 0013 CANCER OF THE EPIPHARYNX: REPORT ON 18 PATIENTS. (E.) Gudnason, D. (Reykjavik, Iceland). *J Laryng* 84(8):795-807, 1970.

A review of the literature on cancer of the epipharynx, which is accompanied by a report of 18 cases, indicates that the frequency of the condition is variable, being low in the white races, but high among the Chinese. Epipharyngeal cancer is more common in men than in women, but is not age-specific; cancers of the epipharynx are prone to metastasize to the lymph glands of the neck. Pathologically, cancer of the epipharynx usually appears as anaplastic squamous epithelial carcinoma or reticular cell sarcoma. Epipharyngeal cancers often present symptoms which mask the true complaint, and diagnosis is often delayed until metastasis has occurred. Most of the patients in the survey of 18 cases presented symptoms of the ear, nose, or cervical lymph nodes (following metastasis). The treatment of choice for epipharyngeal cancer is radiation therapy, although it is usually initiated too late to curb metastasis and early invasive growth, and tumors often recur after radiation treatment has ended. The

5 yr survival rate for epipharyngeal cancer is about 30%. (13 references)

- 0014 CARCINOMA OF THE BREAST: II. THE OTHER BREAST. (E.) Machleder, H. (Stanford U. Sch. Med., San Jose, Calif.). *California Med* 113(3):55-58, 1970.

A patient who has had a radical mastectomy for carcinoma of the breast still has 1 breast which is a target organ for carcinoma. Whether this patient should be subjected to any further treatment or vigilance than the patients in the general population depends on whether or not the chance that carcinoma will develop in this new target organ is more or less or is the same as for her statistical twin who has not had a mammary carcinoma. The indicated probability of developing carcinoma of the breast remaining after mastectomy varies in all studies, but much of this variation may be due to differences in the sample populations examined. A developing carcinoma in a mastectomized patient is more easily detected than in a previously unaffected patient, for the reason that the former patients constitute a more accessible population than the latter. The protective value of preventive simple mastectomy of the remaining breast is unproven, and it is not clear whether the carcinogenic stimulus is more apt to provoke neoplastic change in a remaining breast or in a small nest of residual axillary cells after simple mastectomy. (17 references)

- 0015 LUNG CANCER IN HEMATITE MINERS. (E.) Anonymous. *Lancet* 2(7676):758-759, 1970.

Three possible explanations are advanced for the increased rate of lung cancer observed in hematite miners in Cumberland, England, where it is estimated that hematite miners undergo a risk of contracting lung cancer 70% in excess of the normal population. High levels of radon which have been measured in the iron mines may account for the increased incidence of lung cancer in this population. It is also suggested that iron ore, with its 10% silica content, may be carcinogenic. Although asbestos, a complex silica containing iron, causes mesotheliomas, no mesotheliomas have been observed in iron miners. It is also possible that chemotherapeutic treatment for silicotuberculosis, which was a common cause of death prior to 1950, has left scarred lungs with encysted abscesses which develop into cancer; miners who now survive silicotuberculosis may live on to get cancer. (9 references)

- 0016 AIR POLLUTION AND HUMAN HEALTH. (E.) Lave, L. B. (Grad. Sch. Indust. Admin., Carnegie-Mellon U., Pittsburgh, Pa.), *Science* 169(3947):723-733, 1970.

A detailed review of the literature investigating correlations between air pollution and morbidity or mortality indices is presented. Data on the correlation of pollution and death from lung cancer from England are ambiguous, with some studies indi-

cating that there is a high correlation, and others indicating that correlation is insignificant. Data from the United States support a clear relationship between lung cancer mortality and air pollution, with city-dwelling nonsmokers having death rates between 43 and 120% higher than rural nonsmokers in various studies. Death from stomach cancer is also significantly related to air pollution, as are mortality rates for cancer of the esophagus and bladder. (115 references)

- 0017 SMOKING AND HEALTH. (E.) Fletcher, C. M.
(Roy. Postgrad. Med. Sch., London, England)
and D. Horn. *WHO Chron* 24(8):345-370, 1970.

A survey of the evidence linking smoking and mortality and morbidity from cancer, bronchitis and emphysema, peptic ulcers, heart disease, and tuberculosis indicate that cigarette smokers have an approximately 30-80% greater mortality than nonsmokers, a mortality which peaks in the 45-54 yr age range. More than 30 retrospective and 7 prospective studies have shown that the risk of lung cancer increases directly in relation to number of cigarettes smoked (for heavy smokers the risk is 15-30 times that for nonsmokers). The risk of lung cancer mortality increases with inhalation of smoke, early onset of smoking, taking more puffs on each cigarette, keeping the cigarette in the mouth between puffs, and with relighting half-smoked cigarettes. Mortality rates from lung cancer are lower for women smokers than for men smokers, for smokers of filter cigarettes than for smokers of non-filter cigarettes, and for pipe and cigar smokers than cigarette smokers: and mortality risk declines in those who stop smoking. Environmental factors associated with high lung cancer mortality rates include exposure to urban air components such as coal smoke, occupational exposure to asbestos dust, chromates, nickel, arsenic, radioactive materials, mustard gas, and the products of coal distillation in the gas industry. In all these areas, the risk of lung cancer is largely confined to smokers. Experimental studies have induced cancer in the skin of animals by application of tobacco smoke concentrates; squamous bronchial carcinomas have developed in dogs who had smoked 7 cigarettes per day for 29 months. The carcinogenic agents in tobacco smoke have not been identified, but benzo(a)pyrene is one known cancer initiator which occurs in high concentrations in tobacco smoke. (114 references)

- 0018 CANCER OF THE GALLBLADDER. (Fr.) Girard, M.
M. (Red Cross Hosp., Lyon, France). *J Med Lyon* 51(1189):1361:1372, 1970. (no references)

- 0019 HODGKIN'S DISEASE IN ANIMALS: ITS
RELATIONSHIP TO THE DISEASE IN MAN. (Fr.)
Hoerni, B. (Bergonie Found., Bordeaux, France), E.
Legrand and J. Chauvergne. *Bull Cancer* 57(1):37-54,
1970. (76 references)

- 0020 PERSISTENCE AND ROLE OF ONCOGENIC RNA VIRUS
IN CELL TRANSFORMATION. (Fr.) Vigier, P.
(Fac. Sci. Orsay, France). *Bull Cancer* 57(1):3-12,
1970. (24 references)

- 0021 THE ROLE OF ENDOGENOUS INTERFERON IN THE
DEFENSE MECHANISM AGAINST ONCOGENIC VIRUSES
PRESENT STATE OF OUR EXPERIMENTS. (Fr.) De Maeyer-
Guignard, J. (Fac. Sci. Orsay, France). *Bull Cancer*
57(1):31-36, 1970. (17 references)

- 0022 CHANGES IN TESTICULAR DNA PRODUCED IN BALB/c MICE BY DIETHYLSTILBESTROL. (E.) Uchikawa, T. (Natl. Inst. Radiol. Sci., Anagawa, Chiba-shi, Japan), R. A. Huseby, M. Zain-ul-Abidin and L. T. Samuels. *J Nat Cancer Inst* 45(3):525-533, 1970.

Large doses of diethylstilbestrol (10% content in an 8-10 mg pellet implanted subcutaneously) were administered to male BALB/c mice to investigate an hypothesized direct correlation between estrogens and tumors in the Leydig cells. The DNA content of the cryptorchid testes of treated mice was observed to increase with testicular weight gain, but DNA per unit mass also increased significantly. An increase in DNA secondary to similar treatment with diethylstilbestrol was not seen in (C3H/Bi X A/Bi)F₁ (ZAF₁) mice that have a significantly lower incidence of diethylstilbestrol-induced Leydig-cell tumors or in Holtzman rats in which estrogen-induced interstitial cell tumors have not been reported. Measurements of ³H-thymidine incorporation in the testes of BALB/c mice indicated an early (1-7 days) surge in DNA synthesis that was not detectable in ZAF₁ mice; autoradiographic studies of BALB/c testes demonstrated that this augmented incorporation was primarily, if not entirely, in the interstitial cells. Both quantitative and autoradiographic studies showed that ³H-thymidine incorporation then dropped to levels approaching those of untreated animals until the time of tumor development. Thereafter incorporation increased with the development of pretumorous nodules of interstitial cells, in which DNA synthesis was actively proceeding.

- 0023 CARCINOGENIC PROPERTIES OF ORTHOTOLIDINE (3-3'-DIMETHYLBENZIDINE). (E.) Pliss, G. B. (N. N. Petrov Res. Inst. Oncol., Leningrad, USSR) and M. Zabezhinsky. *J Nat Cancer Inst* 45(2):283-295, 1970.

o-Tolidine (20 mg once a wk) was administered by s.c. implantation or as an oil suspension for 13-14 months to rats in order to test carcinogenic properties. Tumor incidence was 60% in rats given the oil suspension, 64% in rats given the pellets and 78% in rats given pellets which had been subjected to ultraviolet irradiation. Tumors developed mainly in the skin and its related structures, the large sebaceous glands and mammary glands. Biochemical studies showed that subcutaneously administered *o*-tolidine accumulated chiefly in Zymbal's gland, which probably explains the induction of tumors in this organ. Subcutaneous implantation of pellets of *o*-tolidine caused subcutaneous sarcomas in 2 of 68 rats and hepatocellular carcinomas in 4; this effect was not observed when *o*-tolidine was administered as an oil suspension. *o*-Tolidine appears to be a carcinogen with resorptive action, indicating that the carcinogenic effect of this compound may be due to one of its metabolites.

- 0024 INVASIVE TUMORS INDUCED IN RATS WITH ACTINOMYCIN D. (E.) Svoboda, D. (U. Kansas Med Ctr., Kansas City), J. Reddy and C. Harris. *Cancer Res* 30(8):2271-2279, 1970.

Male rats received multiple i.p. or i.v. injections of actinomycin (0.025-0.050 mg/kg) or actinocylgrami-

cidin (0.5 mg/kg) and the resultant invasive tumors were subjected to histological and microscopic examination; the former compound induced invasive transplantable tumors, while the latter did not. The actinomycin-induced tumors appeared as multiple, gray or yellow, firm, irregular, pedunculated, or sessile nodules 2 to 10 mm in diameter attached to peritoneum, mesentery, and serosal surfaces of the abdominal viscera. Invasion into the muscularis of the bowel and, occasionally, infiltration between pancreatic lobules as well as into portal tracts of the liver was also observed. Microscopically, each tumor contained a variety of histological patterns; in most instances, a fibrosarcomatous appearance predominated but, within the same tumors, there were areas resembling hemangioma, dilated cysts, an alveolar pattern, osseous foci, and, in peripancreatic tissue, adenocarcinoma. The tumors had ultrastructural features similar to those reported in mesotheliomas in humans; no insulin-like activity was detected. Solid tumors and ascites forms were transplantable for more than 1 generation. The mechanism of oncogenesis by actinomycin D is probably dependent upon the intact peptone lactone moieties and its binding interactions with DNA.

- 0025 THE EFFECT OF BIOMYCIN ON THE INDUCTION OF HEPATIC TUMORS IN MICE. (Rus.) Pyleva, Z. A. (Acad. Med. Sci. USSR, Moscow) and M. Ya. Vysheslavova. *Biull Eksp Biol Med* 69(6):75-77, 1970.

The effect of biomycin on *o*-aminoazotoluene (OAAT) liver carcinogenesis was studied in 405 CBA x C57BL hybrid male mice. OAAT (1% benzene soln) was applied on shaved portions of intercostal skin 3 times weekly for 11 months (130 applications). Biomycin was administered s.c. for 7 days successively (15 mg/kg daily) at different stages of carcinogenesis, starting 1 wk before OAAT treatment and during the 1st, the 6th and the 26th wk of carcinogen application; the control group received no biomycin. Animals receiving biomycin before OAAT application developed tumors 1 month earlier than the control animals and the groups receiving biomycin during the 1st and the 6th week of OAAT application developed tumors 3 months earlier than the control group. Considerable liver tissue alterations (increase of cellular proportions and mitotic figures) were noticed 1 month from the beginning of the experiment. Atypical alterations of the hepatic cell (polynuclear, giant and irregular cells) occurred later; diffused hyperplasia and hepatocytic hypertrophy produced an overall alteration of the liver structure. All tumors revealed the specific structure of hepatocellular carcinoma. Biomycin enhancement of carcinogenesis was attributed to the presence of the growth stimulating vitamin B₁₂ and to the metabolism stimulating characteristics of tetracyclines.

- 0026 DETECTION OF POTENTIAL WEAK CARCINOGENS AND PROCARCINOGENS: II. CARCINOGENICITY OF TERTIARY BUTYL HYDROPEROXIDE. (E.) Hoshino, H. (Natl. Cancer Ctr. Res. Inst., Tokyo, Japan), G. Chihara and F. Fukuoka. *Gann* 61(2):121-124, 1970.

The effect of topical application of 4-nitroquinoline-1-oxide to female mice and followed by treatment with *t*-butyl-hydroperoxide or *t*-butanol was studied to determine whether the former compound could enhance the carcinogenic activity of the latter 2 compounds. Nine tumors were induced by *t*-butyl-hydroperoxide and only 1 tumor by *t*-butanol when applied after a submanifestational dose of 4-nitroquinoline-1-oxide (20 applications of 0.05 mg in benzene). The difference between the number of tumors produced by these two compounds was statistically significant; the carcinogenicity of *t*-butyl-hydroperoxide is probably due to the production of oxygen-containing free radicals.

0027 TUMORS IN THE URINARY BLADDER OF A MONKEY: INDUCTION WITH 2-NITRONAPHTHALENE. (E.) Conzelman, G. M. (Sch. Vetr. Med., U. California, Davis), J. E. Moulton and L. E. Flanders, III. *Gann* 61(1):79-80, 1970.

2-Nitronaphthalene administration (242 mg/kg p.o.) to a rhesus monkey for 54 months resulted in the formation of numerous papillomas of the urinary bladder when examined at autopsy. The chemical-induced neoplasms were composed of papillae of transitional epithelium which in some areas projected into the underlying lamina propria and submucosa. These epithelial cords showed metaplastic changes, but histopathology consistent with malignancy was not seen. Apparently 2-nitronaphthalene is metabolically reduced in the rhesus monkey and 1 or more of the urinary metabolites has the potential for inducing neoplastic changes in the transitional epithelium of the urinary bladder.

0028 THE EFFECT OF PROLONGED FEEDING OF *ortho*-AMINOAZOTOLUENE ON BINDING TO CELLULAR CONSTITUENTS IN MOUSE LIVER. (E.) Lawson, T. A. (U. Queensland Med. Sch., Herston, Australia). *Chem Biol Interact* 2(1):9-16, 1970.

Female mice received an oral dose of ³H-*o*-aminoazotoluene following a 2-8 wk course of feeding with the unlabeled compound to investigate its binding to nucleic acids and protein in the liver. A rapid decline in the level of binding of labeled material to DNA occurred during the first 2 wk but thereafter the binding remained at a constant level. Binding to protein did not alter significantly during the experiment but there was a continual gradual decline in the binding of labeled material to RNA. Examination of liver DNA, RNA and protein up to 84 days after a single dose of ³H-*o*-aminoazotoluene showed that radioactivity associated with protein could no longer be detected after 28 days whereas that in DNA and RNA was present at 84 days. These results suggest either the existence of a long-lived species of RNA or that the carcinogen stabilizes a species of mouse-liver RNA. Chronic feeding of *o*-aminoazotoluene in the diet for 4 wk reduced the incorporation of ³H-uridine into liver RNA compared with that in untreated mice, although it could not be demonstrated that there was an alteration in the rate of breakdown of RNA.

0029 ELECTRON DENSITY STUDIES ON QUINOLINE ANALOGS OF N,N'-DIMETHYL-*p*-PHENYLAZOANILINE. (E.) Brown, E. V. (Dept. Chem., U. Kentucky, Lexington) and W. H. Kipp. *Cancer Res* 30(8):2089-2090, 1970.

The relationship between electron density and carcinogenic activity of quinoline analogs of *p*-dimethylaminoazobenzene was studied by determining the pK_a of the quinoline nitrogen and the azo nitrogen for the 2-, 3-, 4-, 5-, 6-, 7- and 8-isomers of *p*-dimethylaminophenylazoquinoline. The 5- and 6-isomers which had the highest carcinogenic activity had the highest pK_a values for the amino nitrogen at 2.78 and 2.69, resp., while the other isomers had pK_a's ranging from 0.38-2.39. The pK_a's of the azo nitrogen of the 5- and 6-isomers were 3.36 and 3.37, resp., while the values for the less active isomers fell above and below this narrow range.

0030 BENZENE INDUCED CHROMOSOME ABNORMALITIES IN RAT BONE MARROW CELLS. (E.) Philip, P. (U. Hosp., Copenhagen, Denmark) and M. K. Jensen. *Acta Path Microbiol Scand* 78(4):489-490, 1970.

Rats of both sexes were injected with benzene (2.0 mg/kg, s.c.) 1, 2 and 3 days before sacrifice to determine whether benzene has a direct effect on the chromosome complement of mammalian bone marrow cells. All but 3 treated animals showed an increased number of cell metaphases having structural aberrations consisting exclusively of chromosome breaks, a finding which may suggest that damage occurred in the late S and/or G₂ phases of mitosis. These results indicate that benzene exerts an immediate effect on the chromosomes of mammalian bone marrow cells *in vivo*.

0031 THE RELEVANCE OF CHEMICO-BIOLOGICAL INTERACTIONS FOR THE TOXIC AND CARCINOGENIC EFFECTS OF AROMATIC AMINES: I. CARCINOGENIC ACTIVITY OF SOME 4-AMINOSTILBENE AND 4-AMINOBIENZYL DERIVATIVES. (Ger.) Neumann, H. G. (Max Planck Inst. Biochem., Munich, Germany), M. Metzler, I. Brachmann and C. Thomas. *Z Krebsforsch* 74(2):200-206, 1970.

Stomach-tube-feeding was used to administer 7 amino-stilbene derivatives to rats in an experiment designed to test the carcinogenic activity of these compounds. The known carcinogen trans-4-dimethylaminostilbene (7 μmole twice a week) produced earduct tumors with 100% yields, but equimolar doses of 4-dimethylaminobenzyl and 4-dimethylaminotolane were inactive in 18 months. With cis-4-dimethylaminostilbene no earduct tumors were observed, but weak activity could not be excluded, because one leukemia and one mammary tumor occurred. The chemically reactive derivatives trans-N-hydroxy-4-acetylaminostilbene and trans-N-acetoxy-4-acetylaminostilbene showed the organotropic activity of aminostilbenes in the feeding experiment and produced earduct tumors in females. Although males did not develop any tumors, some died from toxic effects. No carcinogenic or toxic effects were produced by N-acetoxy-4-acetylaminobenzyl.

0032 CANCEROGENIC ALKYLATING SUBSTANCES: III. ALKYL-HALOGENIDES, -SULFATES, -SULFONATES AND STRAINED HETEROCYCLIC COMPOUNDS. (Ger.) Druckrey, H. (Max Planck Inst. Immunobiol., Freiburg, Germany), H. Kruse, R. Preussmann, S. Ivankovic and C. Landschütz. *Z Krebsforsch* 74(3):241-270, 1970.

The carcinogenic efficacy of 12 direct alkylating agents, chosen for chemical reactivity against 4-nitrobenzyl-4-pyridine or for practical use, was tested by administering them s.c., i.v. or p.o., by inhalation, or by the transplacental route to 535 BD-strain rats. S.c. injections once a week of methyl iodide, benzylchloride, dimethyl- and diethyl-sulfate, methyl methanesulfonate, *p*-toluene-sulfonic acid methylester, or trimethylene oxide produced local sarcomas, the yield corresponding to dosage. With di-*n*-butylsulfate, *p*-toluenesulfonic acid ethylester and ethylene sulfide only a few tumors were observed. Veratryl chloride and *p*-toluenesulfonic acid *n*-butylester were not cancerogenic. When given p.o. or by i.v. injections, even dimethyl- and diethyl-sulfate were inactive. Inhalation of dimethyl sulfate vapors, 3 and 10 ppm, resp., for 1 hr 5 times a week, however, produced squamous cell carcinomas of the nasal cavity or neurogenic tumors in 8 of 27 exposed rats. In transplacental experiments a single dose of dimethyl- and diethyl-sulfate was injected into pregnant rats on the 15th day of gestation, with the result that malignant tumors, usually of the nervous system, were developed in 7 out of 59 rats, and in 2 out of 30 of the offspring.

0033 ISLET CELL TUMORS OF THE PANCREAS FOUND IN RATS GIVEN PYRROLIZIDINE ALKALOIDS FROM *AM-SINCKIA INTERMEDIA* FISCH AND MEY AND FROM *HELIOTROPIMUM SUPINUM* L. (E.) Schoental, R. (M. R. C. Toxicol. Unit, Carshalton, Surrey, England), M. E. Fowler and A. Coady. *Cancer Res* 30(8):2127-2131, 1970.

Islet cell tumors of the pancreas developed in rats which had been administered pyrrolizidine alkaloids from *Amsinckia intermedia* Fisch and May (tarweed) and *Heliotropium supinum* Linnaeus, a hepatotoxic Ethiopian plant. One adenoma and 1 adenocarcinoma of the islet cells and 1 adenoma of the exocrine pancreas were found in 3 out of 15 rats given a single dose (500 to 1500 mg/kg) of the pyrrolizidine alkaloids. Among rats treated with *Heliotropium supinum* L., 1 islet cell adenoma was found in 1 of 6 rats given a single dose of its crude alkaloidal fraction (300 mg/kg) and 1 adenocarcinoma in 1 of 2 rats that had the dried plant *H. supinum* in their diet for 1 month. Control rats of ages similar to the test animals did not develop similar tumors.

0034 INFLUENCE OF AGE AND SEX ON CHRONIC THYROIDITIS IN RATS GIVEN SUBCUTANEOUS INJECTIONS OF TRYPTAN BLUE. (E.) Reuber, M. D. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.). *Toxic Appl Pharmacol* 17(1):60-66, 1970.

The influence of age and sex on the incidence of chronic thyroiditis was determined in Buffalo strain rats

(4, 12, 24, and 52 wk of age) given trypan blue (50 mg/kg, s.c. once a wk for 5 wk). Among the female rats the greatest incidence of thyroid lesions occurred in 8-wk-old animals (9/14), 12-wk-old animals (12/14), and 24-wk-old animals (9/14), while among the male rats lesions were more prevalent in 4-wk-old animals (5/12) and 24-wk-old animals (4/12). Thyroiditis was usually moderate in degree (20/37 cases) in female rats and mild (11/19 cases) in males, and severe thyroiditis was observed more often in females (8 cases) than in males (1 case).

0035 EFFECT OF GROWTH OF RHODAMINE SARCOMA IN RAT ON ISOZYMES OF LIVER ENZYMES, WITH REFERENCE TO THE SEESAW CHANGE OF TWO pI-ISOZYMES OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE. (E.) Nakamura, T. (Inst. Protein Res., Osaka U., Japan), Y. Matua, K. Nishikawa, T. Horio and K. Okunuki. *Gann* 61(2):177-190, 1970.

Liver extracts of enzymes from normal and Rhodamine sarcoma-bearing rats were subjected to isoelectric fractionation with Ampholine-carrier ampholytes and divided into their pI-isozymes to investigate the effect of Rhodamine sarcoma growth on liver enzyme isozymes. Glutamate dehydrogenase from normal rats was mostly in a particle-bound form, and divided into at least four fractions of different isoelectric point (pI). The fraction of pI 5.14 (pI 5.14-isozyme) was responsible for most of the total activity, and its activity was hardly influenced by the tumor. There was also a free enzyme, which was so labile as to be totally inactivated during isoelectric fractionation; the activity of the free enzyme was higher in tumor-bearing than normal rats. The enzyme, 6-phosphogluconate dehydrogenase, was resolved into pI 6.16- and pI 6.82-isozymes, and both pI-isozymes were hardly influenced by the tumor until the late stage when pI 6.16-isozyme decreased. Glucose-6-phosphate dehydrogenase was resolved into pI 5.20- and pI 5.90-isozymes; the activity of the former was remarkably higher than the latter in normal rats. With growth of the tumor, the pI 5.20-isozyme decreased and simultaneously pI 5.90-isozyme increased, and the total activity of the two pI-isozymes was not changed by the tumor. The two pI-isozymes of glucose-6-phosphate dehydrogenase showed a strict specificity on glucose 6-phosphate and NADP⁺; neither galactose-6-phosphate nor fructose-6-phosphate acted as a substrate, and NAD⁺ was not substituted for NADP⁺. The *K_m* values of pI 5.20-isozyme and pI 5.90-isozyme were 1.5×10^{-5} M and 6.9×10^{-5} M, resp., for glucose 6-phosphate and 8.4×10^{-6} M and 1.2×10^{-5} M, resp., for NADP⁺.

0036 THE POSSIBLE CARCINOGENIC PROPERTIES OF ALTERED LIPIDS: A STUDY OF PURIFIED COMPOUNDS BY THE NEWT TEST. (E.) Glavind, J. (Central Hosp., Hjørring, Denmark) and E. Arffman. *Acta Path Microbiol Scand* 78(3):345-350, 1970.

The newt test was used as a short-term test for the study of the possible carcinogenic effects of methyl oleate, methyl linoleate and several of their derivatives. The substances were tested in serial dilu-

tions in order to establish dose-response relationships. The most actively necrosis-producing compound was methyl 12-oxo-*trans*-10-octadecenoate. The esters of oleate and linoleate hydroperoxide and the corresponding hydroxy-compounds, obtained by reduction of the hydroperoxides, were also active. Conjugation of the double bonds in linoleic acid gave a weak activity, and the compounds obtained by *trans*-isomerization of the double bonds in oleic and linoleic acid were estimated as inactive. Moderate activity resulted from the introduction of a hydroperoxide or a hydroxyl group in the α -position to a double bond but not in the β -position. The susceptibility of the new to carcinogenic compounds is subject to seasonal variation, with susceptibility increasing in the fall; this factor constitutes an inconvenience attending use of the new test for carcinogenicity.

- 0037 INDUCTION, HISTOGENESIS, AND ISOTRANS-PLANTABILITY OF RENAL TUMORS INDUCED BY FORMIC ACID 2-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]-HYDRAZIDE IN RATS. (E.) Erturk, E. (U. Wisconsin Med. Sch., Madison), S. M. Cohen and G. T. Bryan. *Cancer Res* 30(8):2098-2106, 1970.

Formic acid 2-[4-(5-nitro-2-furyl)-2-thiazolyl]hydrazide-induced renal tubular tumors (0.2% in diet for 46 wk), including cortical (tubular) adenomas, low-grade renal tubular carcinomas, and highly malignant renal tubular carcinomas were transplanted s.c. into weanling female rats to test the malignant potential of these tumors. The chemically induced, small, histologically benign, cortical adenomas demonstrated the same characteristics of cancer as renal tubular carcinomas after 3 serial transplantations. All histologically different tumor lines had the same latent periods, rapid growth rates, and identical histological features with high mitotic activity and extreme cellular pleomorphism when compared with the solid cellular tubular carcinomas. Apparently, formic acid 2-[4-(5-nitro-2-furyl)-2-thiazolyl]hydrazide induces tumors which have many of the properties of cancer and which may be regarded as carcinomas, although they appear benign.

- 0038 COMPARATIVE URINARY AND GALLBLADDER CARCINOGENICITY OF N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]FORMAMIDE AND N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]-ACETAMIDE IN THE DOG. (E.) Erturk, E. (U. Wisconsin Med. Sch., Madison), S. A. Atassi, O. Yoshida, S. M. Cohen, J. M. Price and G. T. Bryan. *J Nat Cancer Inst* 45(3):535-542, 1970.

Six dogs, in 2 groups of 4 and 2, were fed, resp., N-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide and N-[4-(5-nitro-2-furyl)-2-thiazolyl]acetamide, for 2 and 2½ yr, followed by 9 months on a normal diet; the former compound is a urinary bladder carcinogen in mice and rats, the latter a carcinogen for breast, salivary gland, lung and kidney pelvis of the rat and a murine leukemogen. With N-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide, all dogs developed transitional cell carcinoma; half of the dogs developed ureteral transitional cell carcinoma and renal pelvis transitional cell carcinoma. All developed gallbladder

adenocarcinoma and half developed mammary scirrhous carcinoma and mammary fibroadenoma. With N-[4-(5-nitro-2-furyl)-2-thiazolyl]acetamide, all dogs developed gallbladder adenoma and mammary fibroadenoma. The seemingly minor structural difference of the compounds significantly altered the distribution and degree of severity of the tumors.

- 0039 RNA AND AMINE SYNTHESIS IN THE LIVER OF RATS GIVEN INJECTIONS OF THIOACETAMIDE. (E.) Fausto, N. (Div. Biol. Med. Sci., Brown U., Providence, R. I.). *Cancer Res* 30(7):1947-1952, 1970.

The effect of thioacetamide on nuclear RNA metabolism and amine synthesis was investigated in liver homogenates of male rats pretreated with 50-150 mg/kg of the compound (i.p.). A single injection of the drug caused a 38-60-fold increase in ornithine decarboxylase activity which peaked at 24 hr, and a 1.5 to 2.0-fold stimulation of the labeling of nuclear RNA. Puromycin (100 mg/kg) and actinomycin D (2 mg/kg) injections inhibited ornithine decarboxylase activity in thioacetamide-treated rats. Repeated injections of thioacetamide caused accumulation of RNA in the nucleus, increase in the amount of spermidine, and a small decrease in spermine. Organ hypertrophy and increased liver RNA are apparently fostered by parallel changes in RNA and amine metabolism, under experimental conditions.

- 0040 ACCELERATED INDUCTION OF HEPATOMA IN RATS FED N,N'-2,7-FLUORENYLENEBISACETAMIDE BY X-IRRADIATION TO THE TARGET AREA. (E.) Nagayo, T. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan), M. Ito and S. Yamada. *Gann* 61(1):81-83, 1970.

The effects of N,N'-2,7-fluorenylenebisacetamide feeding and X-irradiation on hepatoma growth were studied in Buffalo rats. In macroscopical and microscopical examinations, hepatoma nodules were found within the area exposed to irradiation. Livers of animals fed continuously with N,N'-2,7-fluorenylenebisacetamide were the same as livers of animals with the same diet which were also irradiated. Observations revealed an unstable state of liver parenchyma such as bile ductule proliferation along Glisson's sheath, nodular hyperplasia, cholangiofibrosis, and foci composed of basophilic small hepatic cells, but no malignant changes were observed. The group receiving only X-irradiation alone was found normal, histologically. The duration of the carcinogen feeding was 27 weeks and at this time, no hepatoma was observed in either sex.

- 0041 EFFECTS OF ISOMERS OF ACETOTOLUIDIDE AND AMINO BENZOIC ACID ON THE TOXICITY AND CARCINOGENICITY OF N-2-FLUORENYLACETAMIDE. (E.) Yamamoto, R. S. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda Md.), H. H. Frankel and J. H. Weisburger. *Toxic Appl Pharmacol* 17(1):98-106, 1970.

The *o*-, *m*-, and *p*-isomers of acetotoluidides and aminobenzoic acids were fed to rats at a 44-fold molar

excess dose, to test the inhibitory effect of these agents on carcinogenesis induced by *N*-2-fluorenylacetyl- amide. All 6 compounds tested prevented the death of male Fischer rats due to the toxic action of 300 ppm *N*-2-fluorenylacetyl- amide. However, only *m*-acetotoluidide and *m*-aminobenzoic acid inhibited the carcinogenic effect of *N*-2-fluorenylacetyl- amide, as did acetanilide. *p*-Aminobenzoic acid had a weak inhibitory effect since no hepatomas, but only hyperplastic nodules, were seen. *o*-Acetotoluidide was quite toxic by itself, producing enlarged livers with marked hydropic swelling and fatty changes, whereas *o*-aminobenzoic acid (anthranilic acid) did not lead to liver changes. Hepatoma induction by *N*-2-fluorenylacetyl- amide was not affected by either the two *o*-substituted toluidine derivatives or *p*-acetotoluidide.

- 0042 THE EFFECTS OF 2-ACETYLAMINOFLUORENE AND NITRITE ON FREE RADICALS AND CARCINOGENESIS IN RAT LIVER. (E.) Commoner, B. (Dept. Botany, Washington U., St. Louis, Mo.), J. C. Woolum, B. H. Senturia, Jr. and J. L. Ternberg. *Cancer Res* 30(8): 2091-2097, 1970.

The relationship of the abnormal electron spin resonance signal seen in livers of carcinogen-fed rats to carcinogenesis was investigated. The $g = 2.035$ signal was observed when rats were fed 2-acetylaminofluorene or *p*-dimethylaminoazobenzene in a synthetic (defined and low-protein) diet with 1.6 mg/l of nitrite nitrogen in drinking water, but the signal was absent if the carcinogen was fed in a standard laboratory chow with 32 mg/l of nitrite nitrogen as drinking water. Rats maintained on 2-acetylaminofluorene in synthetic diet and distilled water showed an almost 100% incidence of liver tumors, while animals maintained on 2-acetylaminofluorene on laboratory chow diet had a 50% incidence of tumors. The addition of nitrite to both diets containing the carcinogen decreased the tumor incidence to 63% and 32% in the synthetic and laboratory chow diets, resp. The free radical complex (probably due to a ferrous iron, nitric oxide and a thiol protein complex) appears to be related to a decrease in the carcinogenicity of 2-acetylaminofluorene; the complex formation with cellular thiols may be competitive with that of carcinogen binding to protein thiols.

- 0043 HYDRAZINE TOXICITY IN PREGNANT RATS. (E.) Lee, S. H. (Path. Inst., McGill U., Montreal, Quebec, Canada) and H. Aleyassine. *Arch Environ Hlth* 21(5): 615-619, 1970.

Pregnant female rats were administered s.c. injections of neutralized hydrazine (8 mg/kg/day) for 10 days to assess the toxicity of this compound during pregnancy. The body wt of these treated rats dropped continuously during the experimental period. Fetuses which were examined prior to delivery by termination of pregnancy were characterized by their small size, pallor, and generalized edema, with occasional petechiae. The prenatal and perinatal mortality was 100%. Administration of pyridoxine hydrochloride at 200 mg/kg/day maintained a steady gain of body wt in the pregnant rats but only resulted in partial protection of the fetuses. Intra-

uterine life appears to be more susceptible to hydrazine toxicity than the adult life, and the pathogenesis of the toxicity may be associated with mechanisms other than pyridoxine inhibition.

- 0044 THE EARLY STAGES OF THE 1,2-DIMETHYLHYDRAZINE-INDUCED CARCINOMA OF THE SMALL AND LARGE INTESTINE OF RATS. (Ger.) Springer, P. (Path. Inst. U. Freiburg, Germany), J. Springer and W. Oehlert. *Z Krebsforsch* 74(3):236-240, 1970.

The morphology of intestinal cells in rats undergoing a course of weekly s.c. injections of 21 mg/kg of 1,2-dimethylhydrazine was examined during the early stages of development of intestinal papillomas and carcinomas. In 12 of 77 rats adenocarcinomas developed in the large intestine between the 10th and 16th week after starting the injections. In the same groups 3 carcinomas and 21 papillomas of the small intestine were detected histologically. Autoradiographic investigations after application of ^{34}S -sulfate and ^3H -thymidine revealed alterations of the mucosa of the large intestine characterized by a decrease in the number of mucous secreting cells between the 5th and 12th week of the course of injections. The differentiation of basal epithelial cells in the same region increased, producing an enlargement of the proliferation zone which extended from the bottom of the crypts up to the surface of the mucosa. The labeling index increased 3-fold compared to the normal, and in the small intestine the dedifferentiation zone, being normally identical with the crypts of Lieberkühn, extended the length of the villi. The epithelial cells of the tips of the villi showed a high proliferating activity and a loss of cellular differentiation.

- 0045 EFFECT OF AFLATOXIN B_1 UPON PHYTOHEMAGGLUTININ-TRANSFORMED HUMAN LYMPHOCYTES. (E.) Savel, H. (U. Vermont Coll. Med., Burlington), D. Forsyth, W. Schaeffer and T. Cardella. *Proc Soc Exp Biol Med* 134(4):1112-1115, 1970.

The effects of aflatoxin B_1 on *in vitro* transformation of human peripheral blood lymphocytes by phytohemagglutinin and specific antigens were investigated. Lymphocyte cultures from peripheral blood samples obtained from volunteers containing aflatoxin B_1 , 1.6 $\mu\text{g}/\text{ml}$ in 3% DMSO, and phytohemagglutinin-M, with appropriate controls, were incubated with 50 μC ^3H -thymidine from days 5 to 6 of culture and harvested by filtration on Millipore membranes. The addition of aflatoxin B_1 to phytohemagglutinin-stimulated cultures of human peripheral blood lymphocytes resulted in an inhibition of thymidine uptake as compared to control cultures; the addition of 3% DMSO had no effect on thymidine uptake control cultures. Thymidine uptake in PPD-exposed lymphocyte cultures from a patient who was tuberculin positive was inhibited 62% by incubation with 50 $\mu\text{g}/\text{ml}$ aflatoxin B_1 ; similar inhibition was observed in mumps antigen-exposed lymphocyte cultures from a patient who was mumps-sensitive. When the cultures incubated with phytohemagglutinin and aflatoxin B_1 for up to 4 hr were harvested and the cells washed and placed in new media containing only phytohemagglutinin, the inhibitory effect on

thymidine uptake was not seen. Aflatoxin B₁ apparently blocks a pathway common to both antigenic and phytohemagglutinin stimulation.

0046 LIVER NUCLEAR RNA METABOLISM IN RATS
TREATED WITH AFLATOXIN B₁. (E.)

Friedman, M. A. (Child. Cancer Res. Found., Boston, Mass.) and J. N. Wogan. *Life Sci* 9(13):741-747, 1970.

The dose-dependency characteristics of aflatoxin B₁ inhibition of rat liver polymerase and suppression of precursor incorporation into 28S and 18S nuclear RNA was studied. Liver cell nuclei were isolated from rats treated with 0.5, 1.0 or 3.0 mg/kg aflatoxin B₁, $\frac{1}{2}$, 24 or 48 hr before sacrifice and ¹⁴C-orotate 1 hr before sacrifice. Inhibition of RNA polymerase activity was dose-dependent, rapid and lasted for at least 48 hr; at 5 min after treatment with aflatoxin B₁, there was a 50% inhibition of RNA polymerase activity at each of several levels of ammonium sulfate ranging from 0 to 0.32 M. Nuclear RNA density gradient sedimentation profiles and distribution of radioactivity in fractions of liver nuclear RNA isolated from rats treated with 0.5 mg/kg aflatoxin B₁ showed a marked inhibition of orotate uptake into 28S and 18S nuclear RNA. The alteration of orotate incorporation became progressively more pronounced until all incorporation had virtually ceased by 12 hr after treatment. The relationships of acute responses to aflatoxin B₁ such as these to the mechanisms involved in the chronic response, carcinogenesis, remain to be elucidated.

0047 INTERACTION OF AFLATOXINS B₁ AND G₁ WITH
TISSUES OF THE RAT. (E.) Lijinsky, W.
(U. Nebraska Coll. Med., Omaha), K. Y. Lee and C. H. Gallagher. *Cancer Res* 30(8):2280-2283, 1970.

Groups of female rats were injected i.p. with a solution containing either 1.25 or 0.5 mg of tritium labeled aflatoxin B₁ or G₁ to investigate the incorporation of the carcinogenic aflatoxins into DNA, RNA, and soluble protein of liver, kidney, spleen and intestines. The variation of the amount of incorporation of labeled compound with time was monitored by isolation of nucleic acids and proteins from animals killed 1 hr, 6 hr, 18 hr, 1 week, 4 weeks, and 8 weeks after being given an injection of the labeled aflatoxins. Maximal incorporation of radioactivity into all 3 components of the 4 organs was found between 6 and 18 hr after injection. With both aflatoxins, a progressive decline in specific activity of nucleic acids and protein of the 4 organs was observed from 18 hr to 8 weeks. The highest specific activity with aflatoxin B₁ was in the liver protein at 6 hr, which contained 10% of the injected radioactivity; with aflatoxin G₁, the highest specific activity was in liver RNA at 18 hr. Labeling of kidney and spleen protein was particularly persistent with both aflatoxins, and the radioactivity appeared to be covalently bound to protein. No correlation in the binding of the 2 aflatoxins to DNA, RNA or protein in the various organs and the

higher carcinogenic potency of aflatoxin B₁ compared to aflatoxin G₁ was seen.

0048 STUNTED PIGS FROM SOWS FED CRUDE AFLATOXINS.
(E.) Cardeilhac, P. T. (Dept. Vetr. Sci.,
U. Florida, Gainesville), E. C. Schroeder, J. T.
Perdomo, G. E. Combs and G. T. Edds. *Toxic Appl
Pharmacol* 17(2):548-550, 1970.

A study designed to determine the effects on suckling pigs of aflatoxin administration to the nursing mother is reported. Two sows which had nursing pigs were fed 0.234 and 0.077 mg, resp., of aflatoxin per kg body wt over a 4-day period immediately following parturition. The sow which received the higher level of aflatoxin was sluggish and some serum enzyme values were elevated. Lesions in pigs nursing the sows given aflatoxin, detectable by the methods utilized in these experiments, were mild; however, the pigs from these sows gained weight at distinctly lower rates than control pigs. The stunting was clearly evident by weaning time and persisted until time of slaughter with no compensatory growth seen after weaning. The stunting probably resulted from a transmission of toxin in the milk of the sow to the pigs, rather than from decreased milk production or some other toxic effect on the sow itself.

0049 THE REVERSIBILITY OF INHIBITION OF RNA AND
DNA SYNTHESIS INDUCED BY AFLATOXIN IN RAT
LIVER: A TENTATIVE EXPLANATION FOR CARCINOGENIC
MECHANISM. (E.) Lafarge, C. (Inst. Res. Sci. Cancer,
Villejuif, France) and C. Prayssinet. *Int J Cancer*
6(1):74-83, 1970.

Partially hepatectomized male rats were inoculated i.p. with aflatoxin (250-1000 µg/kg) and subsequently administered 6-¹⁴C-orotic acid to monitor RNA and DNA synthesis. Progressive changes which occurred within a few hr after aflatoxin administration were inhibition of nucleolar RNA synthesis, followed by inhibition of replication and, finally, inhibition of total nuclear transcription. These phenomena were reversible, and the different syntheses recommenced in the following order: after 24 hr total nuclear RNA synthesis was followed by nucleolar RNA synthesis, and DNA synthesis resumed after 48 hr, so that there was a period of at least 24 hr during which RNA was synthesized and DNA was not. The mechanism for the carcinogenic action of aflatoxin may be due to the binding of aflatoxin or one of its metabolites to DNA, with consequent genetic deletions which may lead to malignant transformation.

0050 ON PROTEIN TARGETS OF CHEMICAL CARCINOGENS:
DISSIMILAR MOLECULAR SIZES OF THE PRINCIPAL
PROTEIN CONJUGATES. (E.) Sorof, S. (Inst. Cancer Res.,
Fox Chase, Philadelphia, Pa.), E. M. Young, R. A.
McBride and C. B. Coffey. *Cancer Res* 30(7):2029-
2034, 1970.

The soluble liver protein-carcinogen conjugates produced by feeding 3'-dimethyl-4-dimethylaminoazobenzene (0.058% of diet) or N-2-fluorenylacetamide

0.036% of diet) to adult male rats were resolved and analyzed according to molecular size. The molecular sizes of the principal soluble conjugates of three types of carcinogens were compared in order to deduce whether they originate from a common or similar target protein. The principal conjugate found in the livers of rats given 3'-methyl-4-dimethylaminoazobenzene for 18-21 days consisted of 62% of the soluble protein-bound dyes, belonged to the 5 S class of macromolecules, and was of 60,000 to 80,000 molecular wt. A minor azoprotein (19%) was a 4 S macromolecule (30,000 to 40,000) and was apparently the basic conjugate previously separated on the basis of charge. Small amounts of azo dyes (~5%) were bound to the 2 S (10,000 to 15,000) and ~7.5 S (~150,000) macromolecules. The 7.5 S macromolecule conjugates in livers of rats given *N*-2-fluorenylacetylamide for 5 wk (~150,000) consisted of 40% of the soluble protein-bound Fluorenyl-¹⁴C, and apparently contained the previously described principal charge species, fast and/or slow fluorenyl-¹⁴C-proteins. Each of the other classes of soluble macromolecules had considerably less conjugate. This diversity in molecular wt of the principal isolated conjugates indicates that the target proteins of the 2 carcinogens either are different at least in molecular size or, if identical, are altered in different ways as a result of interaction with the carcinogens.

0051 DIETARY INDUCTION OF SOME ENZYMES OF AMINO ACID METABOLISM FOLLOWING THE ACUTE ADMINISTRATION OF AMINOAZO DYES. (E.) Poirier, L. A. (Hosp. Notre Dame, Montreal, Quebec, Canada) and H. C. Pitot. *Cancer Res* 30(7):1980-1985, 1970.

The effects of 3'-methyl-4-dimethylaminoazobenzene, 2-methyl-4-monomethylaminoazobenzene and *N*-benzoyloxy-4-monomethylaminoazobenzene on the dietary responses of 5 hepatic enzymes, serine dehydratase, histidase, ornithine- δ -transaminase, tryptophan pyrrolase, and tyrosine- α -ketoglutarate transaminase were investigated. Dietary induction was effected by the forced feeding of casein hydrolysate to protein-depleted adult male rats. The i.p. administration of each of the compounds 3 hr prior to the intubation of casein hydrolysate completely inhibited the dietary response of histidase and partially repressed that of serine dehydratase. The metabolic response of ornithine- δ -transaminase was partially repressed by the acute administration of 3'-methyl-4-dimethylaminoazobenzene (50 mg) and 2-methyl-4-dimethylaminoazobenzene (50 mg), but not by *N*-benzoyloxy-monomethylaminoazobenzene (2 mg). Tyrosine- α -ketoglutarate transaminase induction presented an anomalous situation; the injection of 3'-methyl- or 2-methyl-4-dimethylaminoazobenzene 3 hr before enzyme induction had no statistically significant effect upon the induced enzyme level, while *N*-benzoyloxy-4-monomethylaminoazobenzene injected at the same time significantly increased the induced enzyme level. A complete or partial inhibition by 3'-methyl-4-monomethylaminoazobenzene of the induction of serine dehydratase, histidase, and ornithine- δ -transaminase was observed following injection of the dye 16 or 3 hr before, at the same time as, or 3 and 8 hr after the initial intubation of casein hydrolysate. The

injection of dye 16 hr before the start of enzyme induction appeared to inhibit the induction of tyrosine- α -ketoglutarate transaminase; at no time did any of the dyes investigated have a significant effect on the adaptive response of tryptophan pyrrolase. A comparison of these results with the known times of template stability for each of these enzymes suggests that it is during the translational period of enzyme synthesis that 3'-methyl-4-monomethylaminoazobenzene exerts its effects.

0052 METABOLIC ADAPTATIONS DURING HEPATOCARCINOGENESIS: DIETARY INDUCTION OF SOME ENZYMES OF CARBOHYDRATE METABOLISM DURING 3'-METHYL- AND 2-METHYL-N,N-DIMETHYL-4-AMINOAZOBENZENE FEEDING. (E.) Poirier, L. A. (Hosp. Notre Dame, Montreal, Quebec, Canada) and H. C. Pitot. *Cancer Res* 30(7):1974-1979, 1970.

The effects of 0.054% 3'-methyl-4-dimethylaminoazobenzene or 0.054% 2-methyl-4-dimethylaminoazobenzene in the diet following a 3-day fast and a 27-hr re-feeding period with a 30% protein diet on the dietary induction of glucokinase, glucose-6-phosphate dehydrogenase, 6-phosphogluconate dehydrogenase, malic enzyme, and citrate cleavage enzyme were investigated. The metabolic responses of all of the enzymes studied were found to be absent or diminished in the animals fed the 3'-methyl-4-dimethylaminoazobenzene diet for 3 to 5 weeks. Except for 6-phosphogluconate dehydrogenase, the adaptation of which was found to be slightly diminished at the end of 5 weeks of administration of the basal diet the metabolic responses of each of the enzymes in the control animals remained essentially normal throughout the experimental period. The chronic administration of the noncarcinogenic dye, 2-methyl-4-dimethylaminoazobenzene, appeared to produce a loss in the inducibility of 6-phosphogluconate dehydrogenase, a diminished response of glucose-6-phosphate dehydrogenase, and no effect on the metabolic adaptations of the other 3 enzymes investigated. Feeding 3'-methyl-4-dimethylaminoazobenzene appeared to produce an increase in the base level of glucose-6-phosphate dehydrogenase and a marked decrease in the base levels of glucokinase and malic enzyme; the base levels of this latter enzyme were also diminished in the livers of rats fed either 2-methyl-4-dimethylaminoazobenzene or the basal diet. The base levels of all of the other adaptive enzymes tested appeared to be unaffected by any of the diets used in these experiments. The data indicate that, as with rats fed 2-acetylaminofluorene, the normal metabolic responses of the enzymes of carbohydrate metabolism were lost or diminished in the livers of rats fed 3'-methyl-4-dimethylaminoazobenzene.

0053 THE ISOLATION OF NORMAL RAT LIVER *h* PROTEINS AND THE IMMUNOLOGICAL REACTIONS OF MOUSE ANTI-RAT LIVER *h* PROTEIN. (E.) Louis, C. J. (Dept. Path., U. Melbourne, Australia) and J. M. Blunck. *Cancer Res* 30(7):2043-2048, 1970.

Rat liver *h* proteins were isolated from normal rat liver and used to prepare an antibody from mice which was used to study the antigenic proteins from normal, preneoplastic and neoplastic rat liver.

This antibody reacted with normal rat liver *h* proteins and with soluble liver azoproteins from rats fed 3'-methyl-4-dimethylaminoazobenzene but did not react with other soluble proteins from dye-induced rat liver tumors. Immunoelectrophoretic and gel double-diffusion procedures have demonstrated the identity of these *h* proteins with those deleted during azo dye carcinogenesis. The decrease in *h* protein in azo dye-induced carcinomata and the demonstration that an *h* protein antigen cross-reacted with 27% of the azoproteins formed following azo dye administration suggest that the *h* proteins might be a target of the azocarcinogens.

- 0054 EFFECT OF DIETARY RIBOFLAVIN ON AZO DYE REDUCTASE IN LIVER AND IN BACTERIA OF CECAL CONTENTS OF RATS. (E.) Williams, J. R., Jr. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), P. H. Grantham, R. S. Yamamoto and J. H. Weisburger. *Biochem Pharmacol* 19(8):2523-2525, 1970.

The possibility that the bacterial flora in the lower intestinal tract of rats might participate in the metabolism of the carcinogenic azo dye, 4-dimethylaminoazobenzene, was investigated. Azo dye reductase activity was determined in cecal contents and liver homogenates of rats maintained for 6 weeks on a low casein (12%) and low riboflavin (2 ppm) diet or low casein diets to which additional riboflavin was added to give 20 and 200 ppm. With the 2 ppm riboflavin diet, the azo dye reductase activity of the liver was 3.3 nmoles/mg/30 min and 32.7 nmoles/mg/30 min for the cecal contents. Supplementation of the assay mixture *in vitro* with riboflavin raised the activity of both the liver and cecal contents by 16 nmole/mg/30 min. The riboflavin-supplemented diets increased the liver azo dye reductase 7 to 8-fold and the bacterial azo dye reductase by 20-50%. The participation of enzymes provided by the intestinal bacterial flora needs to be considered in studies of the overall fate of exogenous materials in mammalian systems, especially in cases where the compound is either fed orally or secreted into the intestinal tract via the bile.

- 0055 CARCINOGENICITY AND TARGET ORGANS OF METHOXYL DERIVATIVES OF 4-AMINOAZOBENZENE IN RATS: II. EFFECT OF VARIOUS CONCENTRATION OF 3-METHOXY- AND 2,5-DIMETHOXY-4-AMINOAZOBENZENE IN THE DIET. (E.) Odashima, S. (Sasaki Inst., Tokyo, Japan) and Y. Hashimoto. *Gann* 61(2):153-160, 1970.

Two carcinogens, 3-methoxy- and 2,5-dimethoxy-4-aminoazobenzene were administered continuously to male rats (0.09, 0.04, and 0.025% of diet) to assess the tumorigenic properties of these compounds. Liver tumors developed in nearly all of the rats given 3-methoxy-4-aminoazobenzene, but 2,5-dimethoxy-4-aminoazobenzene was essentially non-carcinogenic although 8 times more toxic than the former compound. More extrahepatic tumors were observed in the rats given 0.09% 3-methoxy-4-aminoazobenzene than in those given 0.04% or 0.025% 3-methoxy-4-aminoazobenzene. Among 26 animals receiving 0.09% 3-methoxy-4-aminoazobenzene, tumors of the spleen

and ear duct developed in 3 animals and tumors of the skin and small intestine in 2. With the lower concentrations of 3-methoxy-4-aminoazobenzene, only 2 animals out of 46 developed tumors of the spleen.

- 0056 THE FATE OF N-ALKYL GROUPS IN THE COURSE OF BINDING OF METABOLITES OF SEVERAL N-ALKYL AMINO AZO DYES TO RAT-LIVER PROTEINS. (E.) Matsumoto M. (Fac. Sci. U. Tokyo, Japan) and H. Terayama. *Chem Biol Interact* 2(1):41-45, 1970.

The specific radioactivities of polar dyes prepared from livers of rats 40 hr after administration of N-alkyl-4-aminoazobenzene derivatives (25 mg) in which 1 or the other or both of the N-alkyl substituents had been ^{14}C -labeled, were compared with those of the original azo dyes. The presence of 1 alkyl group was essential for binding to occur; and a metabolite with an N-methyl group was bound preferentially to one with an N-ethyl group. Polar dyes from rats given ^3H and ^{14}C doubly labeled N-methyl-4-aminoazobenzene have the same radioactivity ratios as that of the original non-polar dye, which indicates that the azo dye does not bind at the N-methyl carbon atom, although the presence of the N-methyl group seems to be essential for binding.

- 0057 TUMOR-INDUCED SKIN HETEROGENIZATION: I. RECIPROCAL RELATIONSHIP BETWEEN TUMORS AND SKIN GRAFTS. (E.) Mkheidze, D. M. (Min. Hlth. Georgian SSR, Tbilisi, USSR), A. L. Liozner and G. J. Svet-Moldavsky. *J Nat Cancer Inst* 45(3):465-473, 1970.

Strain-specific tumors were induced in mice and hamsters by i.m. injections of 7,12-dimethylbenz(a)-anthracene to test the reciprocal effect of transplantable tumors and syngeneic or allogeneic skin grafts. When allogeneic skin was grafted to mice before, simultaneously, or after syngeneic tumor implantation, the growth rate of the tumor was unchanged; grafts, taken from tumor-bearing mice, were regularly rejected by normal syngeneic recipients; patterns of rejection were similar to those of common allotransplantation reaction. The rejection of the skin graft may have been caused by the appearance of a new transplantation-type antigen in the skin, which was recognized by an immune mechanism both in syngeneic and allogeneic grafting. Skin grafts, taken from mice that had rejected a skin transplant derived from a tumor-bearing donor, were also rejected in syngeneic transplantation. The "heterogenization state" was successively passed by means of skin transplantation 12 times. Mouse sarcomas induced by 7,12-dimethylbenz(a)anthracene produced skin heterogenization only after being transplanted at least once in syngeneic animals; the skin of primary tumor hosts did not appear to be heterogenized.

- 0058 THE EFFECTS OF 7,12-DIMETHYLBENZ(a)ANTHRACENE ON THE SYNTHESIS OF NUCLEIC ACIDS IN RAPIDLY DIVIDING HEPATIC CELLS IN RATS. (E.) Marquardt, H. (Pharmacol. Inst., U. Cologne, Germany) and F. S. Philips. *Cancer Res* 30(7):2000-2006, 1970.

Young adult rats were partially hepatectomized and injected with an i.v. emulsion of 7,12-dimethylbenz(a)anthracene (25 mg/kg) to investigate the effect of this carcinogen on regenerating liver. The compound administered 24 hr after hepatectomy caused transient (24hr) suppression of regenerative growth, an effect which may be related to carcinogenic activity. The suppression effect was shown by a decrease in mitotic index and inhibition of increases of cell number and total DNA. Similar doses inhibited the incorporation of thymidine-2-¹⁴C and orthophosphate-³²P into DNA of regenerating liver and rapidly growing liver in intact immature rats. The inhibition was evident within 2 hr, maximal by 6 to 12 hr, and no longer present at 24 hr; it was dose dependent and not prevented by adrenalectomy. The incorporation of ¹⁴C-6-orotic acid into rRNA was unaffected. Similar data were obtained when the carcinogen was administered 5 hr after hepatectomy, prior to the onset of DNA synthesis in the regenerating liver. Histological examination of animals treated with 7,12-dimethylbenz(a)anthracene showed no abnormalities. The findings were consistent with a suggestion that 7,12-dimethylbenz(a)anthracene affects DNA primarily in cells in the S phase of the mitotic cycle, possibly by binding to the macromolecule and thus inhibiting its synthesis.

0059 TUMORIGENESIS IN MOUSE SKIN: INHIBITION BY SYNTHETIC INHIBITORS OF PROTEASES. (E.) Carroll, W. (New York U. Med. Ctr., New York), A. Klassen and A. Janoff. *Science* 169(3951):1211-1213, 1970.

Tumorigenesis was initiated in mice by means of exposure to 7,12-dimethylbenz(a)anthracene and promoted with phorbol ester or croton oil to test the inhibition of tumor formation in mouse skin by 3 synthetic inhibitors of proteases: tosyl lysine chloromethyl ketone, tosyl phenylalanine chloromethyl ketone, and tosyl arginine methyl ester. The protease inhibitors were applied in DMSO 3 times weekly in 1.0 µg doses 1-2 hr after croton oil. After 30 wk on promotion, 11 out of 19 control animals (DMSO alone) developed tumors, while only 1 out of 21 animals treated with tosyl phenylalanine chloromethyl ketone, 5 out of 21 animals treated with tosyl lysine chloromethyl ketone and 5 out of 21 animals treated with tosyl arginine methyl ester developed tumors. Some of the irritant effects of the promoter substances were also alleviated by the protease inhibitors.

0060 HORMONE RESPONSIVENESS OF THE TRANSPLANTED TUMORS OBTAINED FROM DMBA-INDUCED MAMMARY TUMORS. (E.) Takahashi, T. (Kyoto Prefect. Coll. Med., Japan) and W. L. Simpson. *Tohoku J Exp Med* 101(1):93-102, 1970.

Male and female rats received transplanted mammary tumors which had originally been induced by 7,12-dimethylbenz(a)anthracene (2.5 mg x 2) to investigate the responsiveness of these tumors to different hormonal environments. Two primary tumors were successfully transplanted into castrated rats receiving estradiol (100 µg) or progesterone (5 mg), and

showed strong hormone responsiveness. The transplanted tumors regressed after withdrawing the hormone, and injection of estradiol and progesterone brought about tumor regrowth after a long period of dormancy. The hormone responsiveness was lost by serial transplantation and metastasis occurred in rats with the hormone-independent tumor. The histologic appearance of the transplanted tumors was greatly altered by hormone; the tumor receiving estradiol showed plump epithelial cells with conspicuous vacuoles and large lumina of acini containing milk-like material. The tumor receiving progesterone displayed fine acini composed of thin epithelial cells, and the regressed tumor exhibited cystic spaces outlined by a single layer of flattened epithelial cells.

0061 CHANGES IN CHROMOSOMES OF BONE MARROW AFTER INTRAVENOUS INJECTIONS OF 7,12-DIMETHYLBENZ(a)ANTHRACENE AND RELATED COMPOUNDS. (E.) Rees, E. D. (U. Kentucky Med. Ctr., Lexington), S. K. Majumdar and A. Shuck. *Proc Nat Acad Sci* 66(4):1228-1235, 1970.

A high incidence of leukemia was induced in rats by i.v. injection (40 mg/kg) of an emulsion containing 7,12-dimethylbenz(a)anthracene (5 mg/ml) or 7,8,12-trimethylbenz(a)anthracene (same dose and same emulsion), with 50% of metaphasic marrow cells showing chromosomes with breaks 24 hr after treatment. Although breaks were inflicted on chromosomes of various sizes and morphology, these aberrations were nonrandom in that members of the nos. 1 and 2 chromosome pairs were involved to an extent greater than expected on the basis of their size and number. Distinctive karyotypic abnormalities involving the no. 2 chromosome were observed in half of the leukemic rats, whereas these abnormalities were not observed in nonleukemic 7,12-dimethylbenz(a)anthracene-treated rats. Fewer breaks in the no. 2 chromosome, and in others, were produced by benzo(a)pyrene and benzo(e)pyrene.

0062 EFFECT OF DIETARY FAT AND DOSE LEVEL OF 7,12-DIMETHYLBENZ(a)ANTHRACENE ON MAMMARY TUMOR INCIDENCE IN RATS. (E.) Carroll, K. K. (Dept. Biochem., U. Western Ontario, London, Canada) and H. T. Khor. *Cancer Res* 30(8):2260-2264, 1970.

7,12-Dimethylbenz(a)anthracene (1, 2.5 or 5 mg p.o.) was administered to female rats which had been maintained on a semisynthetic diet containing 20% corn oil, and to a comparison group which had received a semisynthetic low-fat diet to determine whether dietary fat has an effect on the carcinogenic efficacy of the test compound. The tumor yield (% incidence) was 7%, 57% and 93% in animals given 1, 2.5 or 5 mg of 7,12-dimethylbenz(a)anthracene, resp., with the 20% corn oil diet; with the 0.5% corn oil diet, the tumor yield was 4%, 33% and 70%, resp., for 1, 2.5 or 5 mg of carcinogen administered. The type of diet fed after administration of 7,12-dimethylbenz(a)anthracene had a greater influence on mammary tumor incidence than did the type of diet fed before the carcinogen was given, indicating that the promotional stage of

mammary carcinogenesis is the primary target of the low-fat effect.

- 0063 EFFECT OF 7,12-DIMETHYLBENZ(a)ANTHRACENE ON NON-NEOPLASTIC AND NEOPLASTIC RODENT CELLS IN CULTURE. (E.) Evans, V. J. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), F. M. Price, H. A. Kerr and H. M. De Oca. *J Nat'l Cancer Inst* 45(3): 429-441, 1970.

Neoplastic and non-neoplastic paired cell lines of mouse, rat and hamster were treated with 7,12-dimethylbenz(a)-anthracene *in vitro* to gauge their resistance or susceptibility to the toxic effects of the chemical. Sensitivity to the carcinogen (inhibition of growth) consistently correlated with the non-malignant state, except for freshly explanted mouse embryo tissue. However, long-term cultures of mouse embryo in fetal calf serum acquired sensitivity to the chemical. Data from such cells, usually obtained only after prolonged latent periods in appropriate hosts, are mandatory to confirm whether these cells can produce tumors. The observed correlation between resistance to 7,12-dimethylbenz(a)anthracene toxicity and malignancy in some long-term and freshly explanted cell systems may indicate that the *in vitro* tissue carried over a protective factor from the *in vivo* state.

- 0064 INTERACTION BETWEEN ESTROGENIC AND CARCINOGENIC SUBSTANCES IN THE RAT MAMMARY GLAND. (E.) Sander, S. (U. Hosp., Oslo, Norway) and O. Torgersen. *Acta Path Microbiol Scand* 78(3):289-294, 1970.

Interaction between estrogenic (estradiol-17 β) and carcinogenic (7,12-dimethylbenzanthracene, DMBA) substances was evaluated in the rat mammary gland by determining tumor incidence after DMBA injection (3 mg, i.v.) during the metestrous or proestrous/estrous phases and by measuring ³H-DMBA uptake after estradiol-17 β priming. Tumors were induced in both the metestrous phase (20 adenocarcinomas) and in the proestrous/estrous phase (16 adenocarcinomas), and the 10 animals that did not develop tumors had been in different phases of the estrous cycle when DMBA was applied. Ovariectomy performed when the tumors reached 10 mm diameter produced histological signs of regression in 25 tumors, 8 remained hormone-unresponsive and continued to grow, and 3 were unaffected. Estradiol-17 β -primed animals and controls had the same DMBA uptake, indicating that no competition for intracellular binding sites existed. The development of both hormone-responsive and hormone-unresponsive tumors in the same animal suggests an importance of local factors in hormone-sensitivity in breast cancers.

- 0065 INHIBITION BY GERM-FREE STATUS OF DEVELOPMENT OF LIVER AND LUNG TUMORS IN MICE EXPOSED NEONATALLY TO 7,12-DIMETHYLBENZ(a)ANTHRACENE: IMPLICATIONS IN RELATION TO TESTS FOR CARCINOGENICITY. (E.) Roe, F. J. C. (Roy. Cancer Hosp., London, England) and G. A. Grant. *Int J Cancer* 6(1):133-144, 1970.

The carcinogen 7,12-dimethylbenz(a)anthracene was injected into germ-free male mice shortly after birth to determine if the germ-free condition protected them against tumor formation. Germ-free status significantly protected mice from the early development of liver-cell tumors and from the early development of adenomas of the lung in response to the same treatment, and may have protected 7,12-dimethylbenz(a)anthracene-treated female mice from the development of malignant lymphoma, mammary, ovarian and uterine tumors. Age in excess of 80 weeks counteracted the protective effect of germ-free status. Germ-free status had no consistent effect on the incidence of sarcomas at the site of neonatal injection of 7,12-dimethylbenz(a)anthracene. The fact that a factor as non-specific as the difference between normal microbiological status and germ-free status may have such a profound effect on the age-standardized risk of development of lung and liver tumors in mice, suggests that the term "carcinogen" should not be applied to an agent if the only evidence of relevant activity is that it increases the risk of development of either or both these types of tumors in mice. Germ-free status may influence the response to 7,12-dimethylbenz(a)anthracene by an effect on the host organism's immunological status; the immunological defenses of an animal with no stresses upon its immune system by microbial flora in the environment may be better able to resist cell deviants resulting from exposure to 7,12-dimethylbenz(a)anthracene than those of an animal exposed to the usual complement of microbial flora.

- 0066 STUDIES ON THE METABOLISM OF 7-METHYLBENZ[a]ANTHRACENE AND 7,12-DIMETHYLBENZ[a]ANTHRACENE AND ITS HYDROXYMETHYL DERIVATIVES IN RAT LIVER AND ADRENAL HOMOGENATES. (E.) Sims, P. (Roy. Cancer Hosp., London, England). *Biochem Pharmacol* 19(7):2261-2275, 1970.

The metabolism of tritiated 7,12-dimethylbenz(a)-anthracene, 7-methylbenz(a)anthracene and their hydroxymethyl derivatives was studied with liver homogenates from normal and 3-methylcholanthrene-treated rats. Liver homogenates from rats pretreated with 3-methylcholanthrene converted 7-hydroxymethyl-12-methyl and 12-hydroxymethyl-7-methylbenz(a)anthracene into phenols and dihydrodiols; some hydroxylation of the methyl groups also occurred. Qualitative and quantitative studies of the metabolism of 7,12-dimethylbenz(a)anthracene, 7-methylbenz(a)anthracene and the above hydroxymethyl derivatives showed that with liver homogenates from normal rats products were formed that arise either by ring-hydroxylation or by hydroxylation of the methyl groups, whereas with homogenates of the adrenals from the same animals ring-hydroxylation but little or no hydroxylation of the methyl groups occurred. Adrenal homogenates were more efficient than liver homogenates in effecting the ring hydroxylations of these compounds. Large increases in the amounts of metabolites formed from the above substrates occurred when homogenates of the livers of rats that had been pretreated with 3-methylcholanthrene were used: no such increases were found when homogenates of the adrenals of these animals were used.

0067 INTERACTIONS OF THE K-REGION EPOXIDES OF PHENANTHRENE AND DIBENZ[a,h]ANTHRACENE WITH NUCLEIC ACIDS AND HISTONE. (E.) Grover, P. L. (Roy. Cancer Hosp., London, England) and P. Sims. *Biochem Pharmacol* 19(7):2251-2259, 1970.

The reactivities of phenanthrene-9,10-oxide and dibenz(a,h)anthracene-5,6-oxide with 4-(p-nitrobenzyl)pyridine, RNA, DNA and histone were compared with the parent compounds phenanthrene and dibenz(a,h)anthracene, as well as with alkylating agents such as ethyl methanesulfonate and ethyl methanesulfonate. In neutral solution at 37°C, the K-region epoxides of phenanthrene and dibenz(a,h)anthracene were more reactive towards 4-(p-nitrobenzyl)pyridine than the alkylating agents or their parent hydrocarbons; the epoxides also reacted with DNA, RNA and histone, but the parent hydrocarbons and respective K-region dihydrodiols did not. Addition of washed rat liver microsomes to reaction mixtures containing DNA and either phenanthrene-9,10-oxide or dibenz(a,h)anthracene-5,6-oxide decreased the level of interaction of phenanthrene-9,10-oxide with DNA but not that of dibenz(a,h)anthracene-5,6-oxide. Fluorimetric estimations showed that over a 24-hr period only 1-5% of each epoxide underwent rearrangement to the corresponding phenol and over 90% of the epoxides remained unchanged. The relative stability of a carcinogenic intermediate may be important if the intermediate formed by microsomal metabolism has to enter the nucleus to react with DNA.

0068 THE EFFECT OF ACUTE X-IRRADIATION ON THE CELL PROLIFERATION KINETICS OF INDUCED CARCINOMAS AND THEIR NORMAL COUNTERPART. (E.) Brown, J. M. (Stanford U. Sch. Med., Calif.). *Radiat Res* 33(3):627-653, 1970.

The effect of acute doses of X-irradiation (500 and 1000 rads) on the generation cycle of proliferating cells was compared in chemically-induced (by painting with 7,12-dimethylbenz(a)anthracene squamous cell carcinomas and normal tissue in the cheek pouch of the Syrian hamster using *in vivo* ³H-thymidine labeling (1 µC/g body wt, i.p.) and standard autoradiographic methods. In the unirradiated tumor cells, the mean cell cycle was 11.7 hr, the mean growth fraction (fraction of carcinoma cells proliferating at any one time) was 31%, and the cell loss factor (number of cells lost from the tumor volume) was 0.75. In normal basal cells, the labeled mitosis technique for determining the cell cycle time proved ineffective, and the 3 other methods used (continuous labeling, rate of differentiation of basal cells, and calculation from the equation $T_c = T_s / LI$) gave a range of 130 to 152 hr. Irradiation of the tumor cells with 500 rads did not affect the parameters of the cell cycle although the G₂ period was slightly lengthened (1.8 to 2.6 hr) and the S phase showed greater variation among individual tumors; irradiation with 1000 rads produced a lengthening of the G₁ period (1.8 to 4.5 hr) along with the increased spread of the S phase. Irradiation of normal epithelium with the same doses shortened the cell cycle of the basal cells by 20 to 35% for approximately 3 weeks following irradiation and the effect was due almost entirely to a shortened G₁ period.

0069 STUDIES ON THE KINETICS OF THE INHIBITION OF BENZO(a)PYRENE BREAKDOWN. (Ger.) Tomingas, R. (Med. Inst. U. Düsseldorf, Germany), W. Dehnen and S. Jackson. *Z Krebsforsch* 74(3):279-282, 1970.

The inhibition kinetics of aryl-hydroxylase-mediated benzo(a)pyrene hydroxylation were studied with anthracene, benzo(a)anthracene, benzo(e)pyrene, pyrene, phenanthrene and 3-methylcholanthrene *in vitro*. All these compounds (usually concomitant with benzo(a)pyrene in air dust) inhibited the breakdown of benzo(a)pyrene. Lineweaver-Burk plots revealed a competitive type of inhibition. Application of these findings on the physiological level will be of doubtful value until the mechanism of release of these polycyclic aromatic compounds from the inhaled dust particles is clarified.

0070 INHIBITION OF THE CARCINOGENIC ACTION OF BENZO(a)PYRENE BY FLAVONES. (E.)

Wattenberg, L. W. (U. Minnesota Med. Sch., Minneapolis) and J. L. Leong. *Cancer Res* 30(7):1922-1925, 1970.

Female mice were fed flavone inducers of increased benzo(a)pyrene hydroxylase activity to assess the effect of this treatment on pulmonary adenoma development. The mice were fed inducers for 16 days at 7 weeks and at 11 weeks and each course of treatment was followed by 2 p.o. administrations of 3 mg of benzo(a)pyrene. Three flavones were used: β-naphthoflavone, a highly potent inducer; quercetin pentamethyl ether, intermediate in inducing potency; and rutin, a weak inducer. Administration of β-naphthoflavone (3 mg/g diet) resulted in almost total inhibition of pulmonary adenoma formation; with quercetin pentamethyl ether (5 mg/g diet) approximately 50% inhibition occurred, and with rutin (5 mg/g diet) there was no inhibition. In a second investigation the effect of inducing increased benzo(a)pyrene hydroxylase activity in the skin of mice on epidermal neoplasia initiated by benzo(a)pyrene was studied. More than 50% tumor formation inhibition was achieved by topical application of β-naphthoflavone.

0071 INFLUENCE OF METHYLCHOLANTHRENE AND PHENOBARBITAL TREATMENT ON LIVER CHROMATIN TEMPLATE ACTIVITY IN THE RAT. (E.) Piper, W. N. (Sch. Pharm. Pharm. Sci., Purdue U., Lafayette, Ind.), D. E. Blake and W. F. Bousquet. *Res Commun Chem Path Pharmacol* 1(5):591-606, 1970.

Male rats were given i.p. injections of phenobarbital (100 mg/kg) or 3-methylcholanthrene (30 mg/kg) to investigate the effects of these compounds on liver chromatin template activity. 3-Methylcholanthrene increased hepatic chromatin template activity 100% above control values by 12 hr after administration, whereas phenobarbital or phenobarbital plus 3-methylcholanthrene increased template activity only 10-20%. Treatment of chromatin with acid, to remove basic protein, abolished these differences in template activity; thus, basic protein (histone) appears to be responsible for the difference in chromatin template activity. Similar DNA/protein ratios in chromatin from control and drug-treated

animals indicated that the observed differences in template activity were not due to an alteration in the protein content of chromatin. Adrenalectomy abolished the increase in chromatin template activity produced by phenobarbital treatment, but had no effect on that produced by 3-methylcholanthrene, suggesting that the mechanism by which these agents act to stimulate protein synthesis is different. The ratio of 3-methylcholanthrene bound to chromatin compared to that bound to homogenate protein was considerably larger than that for phenobarbital. Isotope studies established that neither drug caused an alteration in turnover of chromatin-histone protein at 1 or 6 hr after administration, indicating that altered turnover and acetylation of chromatin protein are not responsible for the differences in template activity.

- 0072 QUANTITATIVE DETECTION OF CYTOTOXIC ANTIBODIES AGAINST TUMOR-SPECIFIC ANTIGENS OF MURINE SARCOMAS INDUCED BY 3-METHYLCHOLANTHRENE. (E.) Bloom, E. T. (Dept. Med. Microbiol., Immunol., U. California, Los Angeles). *J Nat Cancer Inst* 45(3): 443-453, 1970.

A murine sarcoma indigenous to the C57BL/10 strain of isogenic mice, and induced by 3-methylcholanthrene, was studied to investigate the antibody response to the tumor-specific antigens associated with it. A new microtechnique was used to detect and assay cytotoxic antibody against tumor-specific antigen, and only microliter quantities of serum were necessary for multiple titrations. The reproducibility of the method was demonstrated at a high level of significance; and the cytotoxic effect depended on the addition of exogenous complement. Furthermore, the detectable antibody titers were specific for the sensitizing sarcoma; antiserum activity resided in the IgG and IgM immunoglobulin fractions. The cytotoxic effect, induced by antigenic stimulation, was boosted with further challenge. This evidence appears to support the conclusion that the cytotoxic effect *in vitro* resulted from a true tumor-specific antibody response.

- 0073 CARCINOGEN-INDUCED TUMORS IN PRIMITIVE PRIMATES. (E.) Adamson, R. H. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), R. W. Cooper and R. W. O'Gara. *J Nat Cancer Inst* 45(3):555-559, 1970.

The carcinogen 3-methylcholanthrene was injected s.c. into 6 tree shrews (*Tupaia glis*) in 10 mg doses to test the susceptibility of prosimians to malignant tumor induction by this agent. Three died within 4 months and the 3 survivors developed fibrosarcomas within 14-16 months. Benzo[a]pyrene was injected s.c. into another species of prosimian primate, *Galago crassicaudatus*. Twelve galagos have survived for more than 6 months after injection of the carcinogen, and 1 developed a tumor at the injection site. Histologically the tumor was a fibrosarcoma, and metastatic tumor was found in the lung. The induction of malignant tumors in higher primates by polycyclic hydrocarbons has proved difficult. It is concluded that some prosimians are more similar

to rodents than to the higher primates in their reaction to carcinogenic polycyclic hydrocarbons.

- 0074 DIURNAL VARIATION IN SUSCEPTIBILITY OF MOUSE SKIN TO THE TUMORIGENIC ACTION OF METHYLCHOLANTHRENE. (E.) Iverson, U. (U. Hosp. Oslo, Norway), O. H. Iversen, H. Hennings and R. Bjerknes. *J Nat Cancer Inst* 45(2):269-276, 1970.

Hairless mice were given a single application of 3-methylcholanthrene (125 µg in benzene) at 0800 and 2400 hr and observed weekly for 20 months to determine if a diurnal variation exists in skin susceptibility to this carcinogen. While no difference was found in tumor induction time or the number of tumor-bearing mice, the group treated at 2400 developed significantly more skin tumors. At 2400, the mitotic rate increased 3-4 times and the number of cells in DNA synthesis increased 40-50% over values found at 0800. The 35% difference in papilloma yield correlates somewhat better with the corresponding difference in number of DNA-synthesizing cells than with the more pronounced variation in mitotic rate. Binding studies with ³H-methylcholanthrene showed 15% higher DNA binding, 10% lower RNA binding and no difference in protein binding after 12 hr with application at 2400 compared to 0800 application.

- 0075 *IN VIVO* ELECTROMETRIC STUDY OF CARCINOGENIC HYDROCARBON INTERACTION WITH MOUSE EPIDERMIS (E.) Smolen, V. F. (Sch. Pharm., Sci., Purdue U., Lafayette, Ind.), D. E. Snyder and R. J. Erb. *J Pharm Sci* 59(8):1093-1098, 1970.

The interaction of the 3-methylcholanthrene and benzene with the epidermis of hairless mice was studied by the use of a bioelectrometric technique involving measurement of electrical potentials developed at the boundary of the affected tissue and a buffer solution which may or may not contain the substances under examination. Use of a bioelectrometric technique permitted experimental results to be obtained entirely *in vivo* without injury to the mice. The results obtained are analogous to titration curves of amphoteric macromolecules. Inspection of the curves and their temporal variations following the topical application of the hydrocarbons revealed the induction of significant changes in the density of ionogenic groups affixed to the epidermal colloids. 3-Methylcholanthrene was observed to induce consistently a reduction (overall average reduction of 23%) of net cationic fixed-charge density attributable to the loss or discharge of basic nitrogenous groups titratable above, at least pH 7.4. Although the mechanism whereby 3-methylcholanthrene reduces the fixed cationic charge density is obscure, it is speculated that the reduction of the charge may result from formation of covalent bonds or from an allosteric mechanism.

- 0076 EFFECTS OF VARIOUS ONCOGENIC AGENTS ON TUMOR-PRODUCING CAPABILITIES OF SERIES D BALB/c MAMMARY NODULE OUTGROWTH LINES. (E.) Medina, D. (Baylor Coll. Med., Houston, Tex.) and K. B. DeOme. *J Nat Cancer Inst* 45(2):353-363, 1970.

The effects of various oncogenic agents (mammary tumor virus, nodule-inducing virus, 3-methylcholanthrene and pituitary isografts) on the tumor-producing capabilities of nodule outgrowth lines D1, D2, D3, D4, D5, D7 and D8 was investigated in BALB/c mice. Fifty percent of the transplants produced tumors in 308, 182, 161, 238, 364 and 168 days in D1, D2, D2a, D3, D4 and D8 lines, resp. Mammary tumor virus infection increased the incidence of mammary tumors and decreased the mean latent period as compared to the same outgrowths transplanted into mammary tumor virus-free BALB/c mice, except for D5. Nodule-inducing virus showed some effect on the tumor potential of line D3 but not of line D3. 3-Methylcholanthrene increased the tumor potential of outgrowth lines D2 and D3 (45% and 60%, resp.); pituitary isografts increased the tumor potential of line D2 (12%). The D series of nodule outgrowth lines appears to show a wide variety of responsiveness to various viral and chemical oncogenic agents and responses cannot be predicted from their background tumor potential.

0077 TRANSFER OF TUMOR-SPECIFIC IMMUNITY WITH RNA: DEMONSTRATION BY IMMUNE CYTOLYSIS OF TUMOR CELLS *IN VITRO*. (E.) Ramming, K. P. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and Y. H. Pilch. *J Nat Cancer Inst* 45(3):543-553, 1970.

Guinea pigs were immunized with a 3-methylcholanthrene-induced strain-2 liposarcoma, and RNA-rich extracts were prepared from their spleens to investigate the mediation of tumor-specific transplantation immunity by such RNA-rich extracts. Normal, nonimmune, strain-2 lymphoid cells incubated with these RNA preparations caused specific immune cytolysis of 3-methylcholanthrene-induced liposarcoma cells *in vitro*. Treatment of the active RNA preparations with ribonuclease resulted in their complete inactivation. RNA from the spleens of guinea pigs not exposed to the tumor was ineffective, and incubation of lymphoid cells with extracts of 3-methylcholanthrene-induced liposarcoma rich in solubilized tumor-specific antigens did not reproduce the immune cytolysis caused by the active RNA preparations. Spleen cells incubated in RNA extracted from strain-2 guinea pigs immunized with 3-methylcholanthrene-induced liposarcoma did not cause significant immune cytolysis when applied to monolayers of MCA-25, a strain-2 sarcoma whose tumor-specific transplantation antigens do not cross-react with 3-methylcholanthrene-induced liposarcoma.

0078 EXPERIMENTAL TUMOR METASTASES AND BLOOD COAGULABILITY. (E.) Hagmar, B. (Dept. Path., U. Goteborg, Sweden). *Acta Path Microbiol Scand* 78(suppl. 211):1-38, 1970.

The relation of blood coagulability to the growth and spread of metastases from transplanted tail tumors in mice was studied using heparin, phenprocoumon, ε-aminocaproic acid (EACA), protamine, and chondroitin sulfate in 3 syngeneic tumor-host systems (3-methylcholanthrene-induced sarcoma, MCG1-SS, and its solid ascites form, MCG1-AS, in CBA mice, and a spontaneous melanoma B16 in C57BL/6J mice). Heparin (100 IU,

s.c.) given 3 times daily from days 7-12 after tumor transplantation increased the average and total volumes of MCG1-SS and MCG1-AS pulmonary metastases and increased the take frequency and total volume of melanoma B16 metastases. Phenprocoumon (0.02 mg, i.p.) reduced the number and total volume of MCG1-SS pulmonary metastases but did not affect MCG1-AS or melanoma B16 metastases. EACA (30% powdered diet) reduced the average and total volumes of MCG1-SS pulmonary metastases, the number and total volume of MCG1-AS metastases, and the average volume of melanoma B16 pulmonary metastases. Treatment with heparin, phenprocoumon, and EACA 6 days after the tumors had been amputated did not significantly affect the growth of metastases on MCG1-SS or MCG1-AS. When treatment was started on days 2 or 3 after tumor transplantation, and the tumors were amputated on day 5, heparin-treated animals had a higher incidence of pulmonary metastases than the other groups, while phenprocoumon and EACA did not alter the time for metastatic spread. When heparin was used on intravenously induced tumors, the number of pulmonary MCG1-SS metastases increased while extrapulmonary metastases were unaltered; the number of extrapulmonary melanoma B16 metastases increased, suggesting that the heparin effect may be a redistribution of tumors. Phenprocoumon increased the extrapulmonary takes and pulmonary B16 metastases, but did not affect pulmonary MCG1-SS metastases. Chondroitin sulfate altered cellular volumes and metastases in a similar manner to heparin, while protamine, a polycation, had rather reverse effects.

0079 INFLUENCE OF MULTIPLE INJECTIONS OF NORMAL SYNGENEIC CELLS ON TUMOR INDUCTION IN MICE. (E.) Reiner, J. (Sloan Kettering Inst. Cancer Res., New York, N.Y.). *Cancer Res* 30(8):2087-2088, 1970.

The effect of injections of normal and X-irradiated syngeneic cells on the oncogenic response to methylcholanthrene in mice was investigated. A series of 50 injections of 0.1 ml of a 10% suspension of normal syngeneic or X-irradiated cells into the right flank at 3- or 4-day intervals did not produce palpable nodules or any noticeable changes. Methylcholanthrene (10 µg i.m.) administered 1 week after the 50th injection of liver cells caused tumor development after 10 weeks. At 52 weeks, 72% of the control mice had developed sarcomas and died, while tumor incidence in mice treated with normal syngeneic liver cells and X-irradiated cells was 53% and 46%, resp. The ectopic injection of normal liver cells presumably activated mechanisms which normally remove necrobiotic cells during renewal and repair of normal tissue, and it may be these same mechanisms can also act to remove neoplastically transformed cells as they arise.

0080 EFFECT OF CUMULATIVE DOSE AND DOSE RATE ON DIMETHYLNITROSAMINE ONCOGENESIS IN RF MICE. (E.) Clapp, N. K. (Oak Ridge Natl. Lab., Tenn.) and R. E. Toya, Sr. *J Nat Cancer Inst* 45(3):495-498, 1970.

The carcinogenic effect of dimethylnitrosamine was assessed in male RF mice given dimethylnitrosamine in drinking water for varying periods, total doses

ranging from 87-243 mg/kg. The incidence of lung adenomas in all treated groups increased over controls by a factor of 2 and reached nearly 100%. The incidence of liver hemangiosarcomas increased in higher dose groups and reached a maximum of 96%, but the incidence of hepatocellular tumors were not affected. In 2 groups receiving the same total dose, hemangiosarcomas appeared only in the group treated at the highest dose rate, which suggested that damage was repaired at the lower dose rate. The fact that lung-tumor incidence with dimethylnitrosamine was high may indicate that metabolism of this chemical into a proximate carcinogen probably occurred in the lung parenchyma as well as in the liver; the absence of tumors in the kidney of the RF mouse suggested that the necessary enzyme system was not present. Because liver hemangiosarcomas and hepatocellular tumors, 2 distinctly different cell types, were induced by dimethylnitrosamine and diethylnitrosamine, resp., the cell type in which metabolism occurs may be specific within an organ.

0081 LIVER MORPHOLOGY FOLLOWING A SINGLE INJECTION OF DIMETHYLNITROSAMINE, 7,12-DIMETHYLBENZ(a)ANTHRACENE, AND URETHAN TO ADULT AND SUCKLING B6AF₁ MICE. (E.) Warwick, G. P. (Roy. Cancer Hosp., London, England) and I. N. Chernozemski. *Chem Biol Interact* 2(1):29-39, 1970.

Adult and 1-wk-old mice received single s.c. injections of dimethylnitrosamine, 7,12-dimethylbenz(a)-anthracene, or urethan with the aim of investigating the effects of these compounds on liver morphology; the injections produced hepatomas in suckling mice but not in adults. Dimethylnitrosamine was highly toxic at a dose of 15 µg/g wt. After treatment with 10 µg/g, less than 10% of the animals died and the rest showed marked congestion and severe centrilobular necrosis accompanied by ascites. The damage was more pronounced in livers of suckling mice where blood-forming cells also disappeared. Slow recovery began during the 2nd wk; undamaged parenchymal cells hypertrophied and some underwent cell division. 7,12-Dimethylbenz(a)anthracene at a dose of 20 mg/g caused mild congestion and parenchymal cell infiltration localized in the middle and outer zones of the lobules. Both effects were transitory and less apparent in suckling mice. Urethan affected small vessels but almost no damage was observed in the parenchyma of the suckling mice (dose 1.2 mg/g). However, blood stem cells exhibited toxic injuries and apparently completely disappeared for about one week. In adults urethan at a dose of 1 mg/g provoked diffuse transitory hydropic vacuolization of parenchymal cell cytoplasm, vessel wall injury, and slight perivascular edema. An inverse correlation was found generally between the hepatocarcinogenicity of the compounds and their liver toxicity.

0082 THE EFFECT OF S-ADENOSYLMETHIONINE ON THE METHYLATION OF LIVER RNA BY DIMETHYLNITROSAMINE *IN VIVO*. (Ger.) Krüger, F. W. (German Cancer Res. Inst., Heidelberg, Germany), U. Rucker and M. Wiessler. *Z Krebsforsch* 74(2):162-170, 1970.

The relation between S-adenosylmethionine and dimethylnitrosamine methylation of guanine in liver RNA was studied by i.v. administration of labeled methionine to control rats and additional high dosage administrations of dimethylnitrosamine (40 mg/kg) to the experimental group; the animals were sacrificed 6 hr after treatment. Concomitant S-adenosylmethionine and dimethylnitrosamine studies were performed on mice. Physiological formation of 7-methylguanine was not competitively inhibited by high doses of dimethylnitrosamine. High doses of S-adenosylmethionine (within its toxicity limits) enhanced formation of 7-methylguanine by labeled (C¹⁴) dimethylnitrosamine methylation. Incorporation of dimethylnitrosamine label into RNA bases was promoted by S-adenosylmethionine in all experimental groups.

0083 A STUDY OF NITROSAMINES AND S-CARBOXYL DERIVATIVES OF CYSTEINE AS LUNG CARCINOGENS IN ADULT SWR MICE. (E.) Mirvish, S. S. (U. Nebraska Coll. Med., Omaha) and L. Kaufman. *Int J Cancer* 6(1):69-73, 1970.

Dimethylnitrosamine, diethylnitrosamine, nitrosopiperidine, di-n-butyl nitrosamine, N-acetyl-S-carbethoxycysteine, S-carbobenzoyloxycysteine and S-carbamylcysteine were injected i.p. into mice to determine their carcinogenic effects on the lung compared to those of urethan. Dimethylnitrosamine (10 mg/kg) and diethylnitrosamine (100 mg/kg) were almost as active as urethan (1 mg/kg). Although the molar dose for dimethylnitrosamine was one-seventh of that for diethylnitrosamine, the former produced the greater effect (8 tumors/mouse vs 5 tumors/mouse). In contrast, for liver carcinogenesis in the rat, diethylnitrosamine is known to be at least as potent as dimethylnitrosamine. Nitrosopiperidine and di-n-butyl nitrosamine showed borderline activities. Similar tests were performed on the urethan metabolite N-acetyl-S-carbethoxycysteine and the related compounds S-carbamylcysteine and S-carbobenzoyloxycysteine, to determine if a cysteine derivative of urethan is responsible for the carcinogenic activity of urethan; no significant tumor induction was observed with these compounds.

0084 CIRCADIAN CHANGES IN THE PERMEABILITY OF NUCLEAR MEMBRANES OF RAT LIVER CELLS FOLLOWING DIETHYLNITROSAMINE ADMINISTRATION. (Ger.) Kittlick, P. D. (Path. Inst. Friedrich Schiller U., Jena, Germany). *Exp Path* 4(2-3):204-206, 1970.

Circadian changes in liver cell nuclear permeability were studied in male Wistar rats treated with diethylnitrosamine for 10 weeks (total 60 mg in drinking water), with daily light exposure from 6 A.M. to 7 P.M.. The animals were sacrificed during the first half of December and experimental data were compared to control data obtained 12 months previously. Pyrophosphate transport was taken as a measure of nuclear permeability and was determined from NAD measurements before and after incubation from the reaction NAD + pyrophosphate = nicotinamide mononucleotide + ATP. Precancerous liver cell nuclei revealed 2 peaks of maximum membrane permeability per 24 hr while control

data showed a single peak in 24 hr. Such alterations were attributed to an enhanced breakdown of certain membrane permeability regulating factors (hormone metabolism) occurring in the preneoplastic cell.

0085 DIETHYLNITROSAMINE CARCINOGENESIS IN RAT LIVER: SORBITOL DEHYDROGENASE HISTOCHEMISTRY. (Ger.) Stiller, D. (Path Inst. Friedrich Schiller U., Jena, Germany). *Exp Path* 4(2-3):207-209, 1970.

decrease in sorbitol dehydrogenase (SDH) activity in rat liver central lobules (diffuse cytoplasmic reaction) was noticed during the first 4 wk of daily diethylnitrosamine administration (0.75 mg in drinking water). A distinct drop in formazan formation in the central lobules occurred on the 10th wk of treatment while total liver SDH activity was still considerable. Clear SDH defective areas appeared between the 12th and 14th wk of treatment (73.5 mg diethylnitrosamine) from which microcarcinomas and carcinomas were generated. Such enzyme defects appeared to be irreversible and were considered as part of the preneoplastic stage in diethylnitrosamine hepatocarcinogenesis.

0086 TUMORIGENICITY OF CYCLIC NITROSAMINES IN SYRIAN GOLDEN HAMSTERS. (E.) Lijinsky, W. (U. Nebraska Med. Ctr., Omaha), A. Ferrero, R. Montesano and C. E. M. Wenyon. *Z Krebsforsch* 74(2):185-189, 1970.

Syrian golden hamsters were given nitrosoazetidine and nitrosoheptamethyleneimine via drinking water (200 mg/l and 50 or 200 mg/l, resp.) to test the carcinogenic effects of these compounds. Although nitrosoazetidine appeared noncarcinogenic in this species, nitrosoheptamethyleneimine was strongly carcinogenic, producing tumors in 21/30 of the animals mainly in the forestomach, esophagus, larynx, pharynx, nasal cavity and trachea. Most of the tumors in the esophagus, larynx, pharynx and nasal cavity were malignant. While nitrosoheptamethyleneimine produced bronchogenic carcinomas in the lungs of rats, it did not induce bronchogenic carcinomas in hamsters.

0087 CARCINOGENICITY OF NITROSTHIOMORPHOLINE AND 1-NITROSOPIPERAZINE IN RATS. (E.) Garcia, H. (U. Nebraska Coll. Med., Omaha), L. Keefer, W. Lijinsky and C. E. M. Wenyon. *Z Krebsforsch* 74(2):179-184, 1970.

The carcinogenic effects of long term feeding to rats of nitrosthioamorpholine and nitrosopiperazine in drinking water (50 mg/l and 200 mg/l) were investigated. Twenty-two of 48 animals treated with nitrosthioamorpholine (760 or 190 mg in 38 weeks) developed tumors of the esophagus and tongue. Nitrosopiperazine treatment (1,200 or 300 mg in 60 weeks) resulted in tumor induction in a wide range of organs and tissues in 22 out of 33 animals; 16 out of 70 of the untreated control rats also developed tumors.

0088 EFFECTS OF DOSE AND SCHEDULE OF METHYLNITROSOUREA ON INCIDENCE OF MALIGNANT LYMPHOMA IN ADULT FEMALE MICE. (E.) Joshi, V. V. (Cancer Res. Lab., U. Western Ontario, London, Canada) and J. V. Frei. *J Nat Cancer Inst* 45(2):335-339, 1970.

Female inbred mice were given single and fractionated doses of methylnitrosourea at daily or weekly intervals to determine the early mortality, incidence and latency of malignant lymphomas induced by this compound. In the single dose group (25-100 mg/kg), early mortality was first seen at 75 mg/kg, the highest incidence of malignant lymphoma was 72%, and the shortest latent period was 144 days. In the fractionated dose group, the pattern of fractionation, (the interval between the fractions) influenced all 3 parameters. In the daily fractionated group, early mortality first appeared at the total dose of 200 mg/kg, the highest incidence of malignant lymphoma was 93%, and the shortest latent period was 139 days. In the weekly fractionated group, early mortality first appeared at the total dose of 250 mg/kg, the highest incidence of malignant lymphoma was 93%, and the shortest latent period was 87 days. Thus reduction of early mortality, enhancement of incidence, and shortening of latent period of malignant lymphoma were the main effects of fractionated doses of methylnitrosourea.

0089 OCCURRENCE OF DESMOSTEROL IN TUMORS OF THE NERVOUS SYSTEM INDUCED IN THE RAT BY NITROSOUREA DERIVATIVES. (E.) Weiss, J. F. (New York U. Med. Ctr., New York), E. G. Paoletti, P. Paoletti, D. Schiffer and A. Fabiani. *Cancer Res* 30(8):2107-2109, 1970.

Desmosterol accumulation in considerable amounts was observed in experimental tumors of the nervous system induced in Long-Evans rats either by i.v. administration of methylnitrosourea or by transplacental induction with ethylnitrosourea. Injections of 25 mg/kg of methylnitrosourea once a month for 8 months in the tail vein of rats induced oligodendrogliomas, isomorphous gliomas, polymorphous gliomas and a few neurinomas; 6.4-16.3% of the total sterols in the oligodendrogliomas was found to be desmosterol. In the series of neoplasms induced transplacentally with ethylnitrosourea (10 mg/kg on the 17th day of pregnancy), a large number of neurinomas of the Gasserian ganglion and spinal neurinomas and a few oligodendrogliomas and 1 polymorphous glioma developed. As in the methylnitrosourea series, the oligodendrogliomas contained 10-14% desmosterol and the neurinomas contained up to 18.5% desmosterol. The presence of this sterol is a fairly constant finding in induced animal neurinomas which are very rapidly proliferating tissues; desmosterol is not found in human neurinomas, which are generally slow growing and rarely malignant, indicating that the presence of desmosterol may be related to the growth velocity of the tumors.

0090 INDUCTION OF NEUROGENIC MALIGNANCIES BY ONE SINGLE DOSE OF ETHYLNITROSOUREA (ENU) GIVEN TO NEWBORN AND JUVENILE BD IX-STRAIN RATS. (Ger.)

Druckrey, H. (Max Planck Inst. Immunobiol., Freiburg, Germany), B. Schagen and S. Ivankovic. *Z Krebsforsch* 74(2):141-161, 1970.

Malignant and multiple tumors of the nervous system were observed in 242 rats at age 1, 10 and 30 days following a single dose of ethylnitrosourea ranging from 5-80 mg/kg. Brain tumors, ependymomas, oligodendrogliomas, astrocytomas, and mixed gliomas were observed in 144 animals, malignant tumors of the spinal cord in 70, of the cranial nerves in 89, and of the parasympathetic nervous system in 140 rats. Nine rats died from tumors of the heart, 7 of which were classified as malignant neurinomas. In all 3 age groups clear dose-response relationships were obtained. The sensitivity of the nervous system to the carcinogenic action of ethylnitrosourea, judged by the tumor yield and the length of the latent period in the respective dosage groups, decreased to about a tenth within the first month after birth, whereas the incidence of nephroblastomas increased with the age at treatment and the dose.

0091 LEUKEMOGENESIS OF N-NITROSOBUTYLUREA IN THE RAT: I. EFFECT OF VARIOUS CONCENTRATIONS IN THE DRINKING WATER TO FEMALE DONRYU RATS. (E.) Odashima, S. (Sasaki Inst. Tokyo, Japan). *Gann* 61(3):245-253, 1970.

Erythroblastic or stem-cell type leukemias were induced in 3 groups of female rats by the administration in drinking water of N-nitrosobutylurea (0.01, 0.02, or 0.04% soln); a higher percentage (76 and 100%, resp.) of leukemias were induced in the groups receiving 0.02 and 0.04% soln. Lesions and tumors induced in other organs included: hyperkeratosis of the forestomach, papillomas and basal cell carcinomas of the forestomach and esophagus, ear duct carcinomas, mammary adenocarcinoma, reticulum cell sarcoma, and adenomatous polyp of the small intestine. More extrahematopoietic tumors were found in the animals that received the lowest daily dose of N-nitrosobutylurea. A higher frequency of leukemia was produced earlier in the experimental period (19-23 wk) by 0.04% of N-nitrosobutylurea, and more extrahematopoietic tumors were produced later (34-45 wk) by the 0.01% concentration.

0092 LEUKEMOGENIC AND MAMMARY TUMORIGENIC EFFECTS OF N-NITROSOBUTYLUREA IN MICE AND RATS. (E.) Yokoro, K. (Res. Inst. Nucl. Med. Biol., Hiroshima U., Japan), N. Imamura, S. Takizawa, H. Nishihara and E. Nishihara. *Gann* 61(3):287-289, 1970.

The leukemogenicity of N-nitrosobutylurea was investigated in mice as well as in rats to learn more about the effect of species and strain differences on the response of the host to the carcinogen. Male and female C57BL/Ka mice, 1-2 months of age, were given 1 mg of N-nitrosobutylurea daily for 115 days; female ICR/JCL received 2-5 mg for a shorter time; all females and 90% of the males developed lymphoblastic leukemia which originated in the thymus with or without general spread, and which was transplantable to adult syngeneic recipients by i.p. inoculation of leukemia

cells. A slight or moderate degree of sustained hypoplasia in both myeloid and lymphoid systems accompanied by a lowering of the immunological competence was observed during the incubation period. Male and female inbred ACI rats, 2 months of age, kept on 5 mg/day of N-nitrosobutylurea for 125 days, developed leukemia (90%) with little or no evidence of thymus and lymph node involvement. No leukemia occurred in 10 female W/Fu rats which had been treated with the carcinogen, but all 10 animals developed mammary adenocarcinomas between 127 and 200 days after the start of N-nitrosobutylurea administration.

0093 EFFECT OF STRESS ON FORMATION OF STOMACH TUMOR IN RATS BY N-METHYL-N'-NITRO-N-NITROSOGUANIDINE. (E.) Takahashi, A. (Natl. Inst. Hyg. Sci., Tokyo, Japan), K. Onoda, K. Kawashima, R. Kato, Y. Omori and M. Ishidate. *Gann* 61(3):295-296, 1970.

The relationship between stomach cancer and stomach ulcer was investigated by feeding a carcinogen, N-methyl-N'-nitro-N-nitrosoguanidine, to rats in which stomach ulcers had been induced by acute stress. Rats given 0, 30 mg/l or 90 mg/l of the carcinogen in drinking water but which were not subjected to stress did not develop any tumors in the stomach and intestine; rats receiving no carcinogen but subjected to acute stress (immobilization in a stress-cage and immersion in 23°C water for 16 hr) developed ulcers in the glandular stomach, but no tumors were observed. Solid tumors in the glandular stomach were observed in all rats subjected to stress and carcinogen treatment. One or more adenomatous hyperplastic nodules and fibrosarcomas developed in the stomach (3-6 mm diameter) and in the duodenum (5-20 mm diameter).

0094 ELECTRON MICROSCOPIC STUDIES ON CULTURED RAT LIVER CELLS TRANSFORMED BY 4-NITROQUINOLINE-1-OXIDE. (E.) Koshiba, K. (Okayama U. Med. Sch., Japan), M. Namba and T. Oda. *Gann* 61(3):233-238, 1970.

Liver cell cultures from male rats were exposed to 10^{-6} M 4-nitroquinoline-1-oxide; electron microscopy was performed on control cells, carcinogen-transformed test cells, solid and ascites tumors produced by i.p. back-transplantation of the transformed cells, and cells cultivated from the ascites tumor. The control cells probably originated from hepatic parenchymal cells. However, no specific features of liver cells *in vivo* were observed in the control liver cells in long-term culture and identification of the cultured liver cells was unsuccessful. The electron microscopic studies on the 4-nitroquinoline-1-oxide-transformed cells revealed vacuolization of Golgi bodies, irregular nucleus, and swelling of rough endoplasmic reticulum and mitochondria. The ultrastructural observation of the control cells and the tumor cells transformed by 4-nitroquinoline-1-oxide indicated that a mixed population of cells with different origin, at least two kinds of cells, the liver cells and the cells other than liver cells, were contained in the culture originating from the rat liver tissues. It appears from these findings that these two kinds

f cells are transformed in culture by 4-nitroquinoline-1-oxide and that the tumor produced by the back-transplantation of cells treated with the carcinogen contains the 2 types of cells.

0095 EFFECT OF ALKYL BENZENESULFONATE AS A VEHICLE FOR 4-NITROQUINOLINE-1-OXIDE ON GASTRIC CARCINOGENESIS IN RATS. (E.) Takahashi, M. (Med. Sch. Nagoya City U., Japan). *Gann* 61(1): 7-33, 1970.

The effect of alkylbenzenesulfonate as a vehicle for 4-nitroquinoline-1-oxide on gastric carcinogenesis was studied in rats. Rats were divided into groups which were given (by esophageal intubation) 1 mg of 4-nitroquinoline-1-oxide in 1 ml of 0% ethanol with 8% alkylbenzenesulfonate 2-3 times a week for 18 weeks, or the same dose in 1 ml of 0% ethanol alone, or 1 ml of 20% ethanol with 8% alkylbenzenesulfonate without 4-nitroquinoline-1-oxide for controls. No neoplasms of the stomach or other organs were seen in the controls. Of 15 treated animals in the first group, 2 adenocarcinoma, 1 hemangiosarcoma, 1 hemangioma, 2 cases of atrophic gastritis, papillomas of the forestomach, 5 squamous cell carcinomas, and 2 giant squamous cell papillomas were found. In the group with the carcinogen without the surfactant, only benign papillomas of the forestomach were found in 9 rats and 1 case of liver sarcoma was found. The surfactant alkylbenzene sulfonate appeared to increase the carcinogenicity of 4-nitroquinoline-1-oxide.

0096 INHIBITORY EFFECT OF ALUMINUM ON THE DEVELOPMENT OF EXPERIMENTAL LUNG TUMOR IN MICE INDUCED BY 4-NITROQUINOLINE-1-OXIDE. (E.) Kobayashi, T. (Sch. Med., Chiba U., Japan), H. Katsuki and Y. Iizumi. *Gann* 61(3):239-244, 1970.

The effect of aluminum compounds on the development of experimental lung tumors induced by 4-nitroquinoline-1-oxide was investigated in female dd strain mice. Prior to s.c. injection with 0.25 mg of 4-nitroquinoline-1-oxide once a week for 5 weeks, the animals were made to inhale 0.2% $AlCl_3$ solution or Al_2O_3 daily for 1 week; further inhalation was continued twice a week for 7 months after the 4-nitroquinoline-1-oxide treatment. In animals treated with $AlCl_3$ or Al_2O_3 and 4-nitroquinoline-1-oxide, 60% and 70%, resp., of the animals developed a small lung adenoma without development of adenocarcinoma. All animals treated with 4-nitroquinoline-1-oxide alone developed multiple lung adenoma and 2 animals developed adenocarcinoma. The results indicate that the incidence of lung adenoma declined with the administration of aluminum, and that aluminum may inhibit the induction of adenomatous change in the lungs of mice by 4-nitroquinoline-1-oxide.

0097 CHROMOSOME ABERRATIONS AND PERSISTENT NUCLEOLI OF YOSHIDA SARCOMA CELLS INDUCED BY 4-NITROQUINOLINE-1-OXIDE *IN VITRO*. (E.) Sasaki, H. (Sasaki Inst., Tokyo, Japan). *Gann* 61(2): 193-196, 1970.

The treatment of cultured rat Yoshida sarcoma cells with 4-nitroquinoline-1-oxide (10^{-8} M) induced chromosome aberrations and persistent nucleoli. Examination of 958 metaphase cells (471 treated with 4-nitroquinoline-1-oxide, 487 control cells) showed more increased chromatid gap, chromatid break and chromatid exchange in the carcinogen-treated cells. The occurrence of chromatid break reached the highest level at 13 culture hr and then decreased gradually. The high frequency of chromatid exchange was seen during the decreasing period of the break, showing a gradual rise with the maximum at 30 culture hr and then decreased. After 48 hr, the frequency of chromosome aberrations in the carcinogen-treated group was at the same level as that in the control. Cytopathological examinations of 4-nitroquinoline-1-oxide-treated cells revealed prominent nucleoli in late prophase, prometaphase and metaphase cells within 30 hr when the chromosome aberrations were frequent.

0098 CHROMOSOMAL ALTERATION AND THE DEVELOPMENT OF TUMORS: XX. CHROMOSOME CHANGE IN THE COURSE OF MALIGNANT TRANSFORMATION *IN VITRO* OF HAMSTER EMBRYONIC CELLS BY 4-NITROQUINOLINE 1-OXIDE AND ITS DERIVATIVE, 4-HYDROXYAMINOQUINOLINE 1-OXIDE. (E.) Yosida, T. H. (Natl. Inst. Genet., Shizuoka, Japan), T. Kuroki, H. Masuji and H. Sato. *Gann* 61(2):131-143, 1970.

Golden hamster embryonic cells were transformed to malignancy *in vitro* by treatment with 4-nitroquinoline-1-oxide and its derivative, 4-hydroxyaminoquinoline-1-oxide ($4 \times 10^{-5.5}$ and $10^{-4.5}$ M, resp.), and the chromosomes were examined with special regard to karyotype change in different stages of malignant transformation. In 5 of 11 transformed cell lines the chromosome numbers had a tetraploid mode, a diploid mode in 4, and in the remaining 2 the distribution was bimodal with a tetraploid and a diploid peak; one spontaneously transformed line showed a hyperdiploid mode. Generally, cells at an early stage of malignant transformation by carcinogen treatment had diploid or near-diploid chromosome number, but at later stages after transformation they had near-tetraploid chromosome numbers. Karyotypes of cells with diploid chromosome number, however, deviated more or less from those of normal somatic cells. The first event of cell transformation on the chromosomal level seems to consist of structural chromosome changes, such as gaps, breaks, and deletion, whereupon heteroploid and polyploid karyotype changes follow due to non-disjunction and/or duplication of chromosome sets.

0099 INFLUENCE OF THYMECTOMY, SPLENECTOMY, AND CORTISONE ON CARCINOGENESIS. (It.) Della Porta, G. (Natl. Tumor Inst., Milan, Italy), M. I. Colnaghi and L. Parmi. *Tumori* 56(2):121-135, 1970.

The effects of thymectomy, splenectomy and cortisone treatment on urethan carcinogenesis in mice were studied in 3 experiments; and the effect of thymectomy on tumor incidence without a urethan treatment was studied in a 4th experiment. Groups of outbred

albino CTM mice were either thymectomized or splenectomized at 4 weeks of age and administered urethan 0.4% in drinking water for 10 days at 5 weeks. In comparison with intact, urethan-treated animals, the thymectomized, urethan-treated mice had a slightly lower incidence of malignant lymphomas (19% vs 24%), a marked decrease of mammary tumors (31% vs 62%), and increased incidence of lung adenomas (84% vs 48%) and of skin papillomas (10% vs 1%). Thymectomized, but otherwise untreated mice developed less lymphomas and mammary tumors than intact, untreated controls, while splenectomy did not modify significantly the tumor incidence. In a second experiment, groups of CTM mice were administered either 1 mg of cortisone s.c. daily for 10 days or urethan in the drinking water for 5 days followed by 5 days of cortisone or vice versa, or urethan alone. No major differences in the tumor incidence in the various groups were observed, apart from a decreased incidence of thymic lymphosarcomas in the group with cortisone after urethan. In a third experiment, CTM mice were given 2 mg urethan within the 1st day after birth and thymectomized or sham-operated; both groups had a high incidence of hepatomas and lung adenomas, and developed only few lymphomas and mammary tumors. In the fourth experiment, the C3H mice thymectomized at birth developed fewer hepatomas and mammary tumors than sham-operated animals.

- 0100 TUMOR INDUCTION WITH SINGLE URETHAN INJECTION IN NEWBORN AND ADULT SYRIAN GOLDEN HAMSTERS: A STUDY ON AGE INFLUENCE. I. (E.) Toth, B. (U. Nebraska Coll. Med., Omaha). *Int J Cancer* 6(2):63-68, 1970.

The administration of urethan (1 mg/kg s.c.) to Syrian golden hamsters (newborn and 8 wks old) caused a higher incidence of forestomach papilloma in animals receiving urethan as adults (33%) than at birth (23%). Urethan administration gave rise to similar incidences of dermal melanocytomas in the 2 age groups. Other tumors were also observed in the animals. Since only a few were seen of each type, it is difficult to relate their appearance to the treatments. It is concluded that age is a factor in the oncogenic response of golden hamsters challenged by a single chemical stimulus.

- 0101 RECOVERY FROM THE INHIBITORY EFFECT OF X-RADIATION ON URETHAN LUNG ADENOMAGENESIS. (E.) Bartlett, G. (Inst. Cancer Res., Fox Chase, Philadelphia, Pa.). *Int J Cancer* 6(1):56-62, 1970.

The reversibility of radiation-induced inhibition of urethan lung tumors was studied in male (C₃HfB/He x A/He)F₁ mice irradiated with 500 r 24 hr or 2 weeks prior to the administration of urethan for 3 days. After 260 days, thymectomized, urethan-treated mice developed an average of 6.8 tumors each, while mice irradiated 24 hr prior to urethan treatment developed only 2.1 tumors each. Animals irradiated 2 weeks prior to urethan administration developed an average of 4.8 tumors each; thymectomized mice which had been irradiated 2 weeks prior to urethan treatment developed 5.6 tumors each. The immunity to urethan-induced tumors conferred by a sublethal dose

of radiation seemed to be transient and the recovery process was not dependent on the thymus.

- 0102 CHROMOSOMAL ALTERATION AND DEVELOPMENT OF TUMORS: XXI. CYTOGENETIC STUDIES OF PRIMARY PLASMA-CELL NEOPLASMS INDUCED IN BALB/c MICE. (E.) Yoshida, T. H. (Natl. Inst. Genet., Misima, Japan), H. T. Imai and K. Moriwaki. *J Nat Cancer Inst* 45(3):411-418, 1970.

Intraperitoneal injection of 0.5 ml of Freund adjuvant produced plasma cell tumors in the peritoneum of 19 mice; chromosomal studies were performed on 14 primary tumors. Of these, 3 had diploid, 1 had hypodiploid (44), and the remaining 10 had hypotetraploid or hypertetraploid chromosomes. In tumors developing shortly after treatment, diploid or near-diploid cells were more frequent, whereas in those appearing a long time after treatment, polyploid cells were more frequent. Diploidy of primary tumors changed to near-tetraploidy after 1-2 transplant generations. Mouse plasma cell tumors can apparently develop from cells with diploid chromosome numbers, but then can change to aneuploidy during further growth.

- 0103 THE USE OF CARRAGEENAN AS A GRANULOMA-PRODUCING AGENT IN FREUND'S ADJUVANT. (E.) Salvaggio, J. (Louisiana St. U. Med. Sch., New Orleans) and V. Kundur. *Proc Soc Exp Biol Med* 134(4):1116-1119, 1970.

Carageenan was substituted for mycobacteria in complete Freund's adjuvant and observations on antibody production and delayed hypersensitivity to crystalline bovine serum albumin were made on guinea pigs. The carageenan-Freund's adjuvant administered in dose ranges of 0.025-2.5 mg resulted in marked reduction in intensity of delayed hypersensitivity to incorporated protein antigen (4-9 mm of induration and erythema); *M. tuberculosis* adjuvant reactions ranged from 10-27 mm. Carageenan also failed to enhance γ 2 anti-BSA titers (20-160), when compared with mycobacterial adjuvant (640-5120). Animals receiving carageenan developed small draining nodes in contrast to the large hypertrophied and hyperplastic nodes after mycobacterial adjuvant.

- 0104 PROGRESS REPORT ON STUDY OF RESPIRATORY SPIRALS. (E.) Walker, K. R. (Holy Cross Hosp., Salt Lake City, Utah) and C. D. Fullmer. *Acta Cytol* 14(7):396-398, 1970.

The incidence of Curschmann respiratory spirals in the sputum of cigarette smokers was investigated. The sputum and smoking histories of 20 patients were examined and compared to see if there was a relationship between the amount smoked and numbers of spirals produced. Spiral counts ranged from 1 to 916 spirals per aliquot of sputum. However, although 94% of the smokers produced spirals, no direct or general rise in numbers of spirals was seen as the amount and number of years smoked increased.

- 0105 CARCINOGENIC EFFECT OF CIGARETTE TAR USING NEWBORN ICR MICE. (E.) Takayama, S. (Cancer Inst., Tokyo, Japan). *Gann* 61(3):297-298, 1970.

The carcinogenic effect of cigarette tar in newborn mice was investigated by s.c. injection of 0.025 ml or 0.05 ml of a 10% olive oil solution of tar in the interscapular region within 24 hr after birth or an injection of 0.05 ml of olive oil as control. Twelve out of 20 mice injected with 0.025 ml of the tar solution, and 16 out of 26 mice receiving 0.05 ml of the tar solution developed tumors of the liver, lung and lymphoma; control mice had a tumor incidence of 4 in 6.

- 0106 THIN-LAYER CHROMATOGRAPHY OF 4-(4'-NITROBENZYL)-PYRIDINE-REACTIVE COMPOUNDS IN TOBACCO SMOKE. (E.) Norpoth, K. (Hyg. Inst. U. Munster, Germany) and T. Papatheodorou. *Naturwissenschaften* 57(7):356, 1970.

Tobacco smoke condensate was fractionated by thin-layer chromatography and reacted with 4-(4'-nitrobenzyl)pyridine to detect alkylating activity. A 4-(4'-nitrobenzyl)pyridine-positive band was detected in the water-soluble portion of the tobacco smoke condensate; extracts of tobacco did not contain this compound. Five or more other 4-(4'-nitrobenzyl)pyridine-positive bands were found in the neutral ether extracts of both the tobacco smoke and tobacco extracts.

- 0107 *IN VIVO* AND *IN VITRO* CILIOTOXIC EFFECTS OF TOBACCO SMOKE. (E.) Dalhamn, T. (Inst. Hyg., U. Uppsala, Stockholm, Sweden). *Arch Environ Health* 21(5):633-634, 1970.

Tobacco smoke exposure in doses ("puffs") of 1 ml and 10 ml produced ciliostasis in rabbit trachea *in vitro* and in cat trachea *in vivo*. One ml exposure required 3 puffs and 71 puffs to produce ciliostasis in rabbit trachea and cat trachea, resp. In the experiments with 10 ml puffs, 37 puffs and 35 puffs were required to produce ciliostasis. Since it is apparently a matter of indifference in the production of ciliostasis whether the *in vivo* or the *in vitro* technique is used, the method of preparing trachea specimens might be simplified to permit *in vitro* techniques and the use of fewer animals.

- 0108 OF BEAGLES, SMOKING, AND CANCER. (E.) Anonymous *Roche Med Image Comment* 12(7):1-13, 1970.

Two related studies designed to induce lung cancer in beagles by cigarette smoking are reported; cigarette smoke was pumped into the beagles' lungs through tracheostomy tubes. In a pilot study using 10 beagles, after 420 days of heavy smoking, epithelial lesions were observed in the lungs of most dogs, lesions which may form a phase in the development of carcinoma *in situ*. In the full scale study, 86 beagles smoked filter and nonfilter cigarettes for as long as 875 days, with the result that invasive bronchioalveolar tumors were observed, as were early

invasive squamous cell carcinomas of the bronchii similar to those observed in the lungs of humans with lung cancer. Tumor formation was directly correlated with number of nonfilter cigarettes smoked; beagles smoking filter cigarettes had a lower rate of tumor incidence per number of cigarettes smoked than beagles smoking nonfilter cigarettes.

- 0109 MORTALITY IN SMOKING DISCORDANT MONOZYGOTIC AND DIZYGOTIC TWINS: A STUDY ON THE SWEDISH TWIN REGISTRY. (E.) Friberg, L. (Karolinska Inst., Stockholm, Sweden), R. Cederlof, T. Lundman and H. Olsson. *Arch Environ Health* 21(4):508-513, 1970.

Data on mortality, including cause of death, in smoking discordant monozygotic and dizygotic twin pairs from Sweden showed an excess mortality among male dizygotic smokers that was not associated with any specific cause of death. The 4 cases of death from lung cancer among dizygotic men occurred only among smokers; the 1 case of lung cancer mortality in the monozygotic group occurred in the nonsmoking twin. Other forms of cancer accounted for 8 deaths among dizygotic male smokers, and for 3 deaths among dizygotic male nonsmokers. Among women, death from lung cancer occurred only in the case of 1 subject, a dizygotic smoker, and deaths from other cancers occurred in 8 nonsmoking dizygotic twins, and in 7 smoking dizygotic twins. Monozygotic women accounted for 3 deaths from cancers other than lung cancer in both the smoking and nonsmoking categories.

- 0110 CANCER OF THE BLADDER IN PATIENTS TREATED WITH CHLORNAPHAZINE. (E.) Laursen, B. (Gentofte Hosp., Copenhagen, Denmark). *Brit Med J* 3(5724):684-685, 1970.

The development of cancer of the bladder in 2 women who had, 5 and 6 yr previously, been treated with chlornaphazine for Hodgkin's disease, is reported. In both cases, X-irradiation had also been used in treating the original complaint, with irradiation affecting the pelvic lymph nodes in 1 case, and the neck, axillae, supraclavicular regions and mediastinum in the other case. Biopsies of the bladder revealed papillomatous carcinoma grade I in 1 case, and an atypical epithelium and urothelium corresponding to a grade III noninvasive carcinoma in the other case. Chlornaphazine is thought to be the most likely cause of bladder cancer in the 2 cases.

- 0111 HEALTH CONSIDERATIONS IN THE USE OF ORGANIC REACTOR COOLANTS. (E.) Weeks, J. L. (Whiteshell Nucl. Res. Estab., Pinawa, Manitoba, Canada) and B. C. Lentle. *J Occup Med* 12(7):246-252, 1970.

The toxicity and carcinogenicity of terphenyls, which are used as comparatively inexpensive organic coolants in nuclear reactors, were studied in 47 persons exposed to the organic coolant for periods of at least 6 months to 7 yr and in 47 matched

controls. The exposure group showed no untoward incidence of tumor formation. Pulmonary function, hematological investigations, and serum isocitric dehydrogenase levels were the same in both groups. Although observation over a longer term will be necessary to determine any carcinogenic effects of terphenyl, available information does not suggest that this will be a likely hazard.

- 0112 CHROMOSOME DAMAGE AFTER OCCUPATIONAL EXPOSURE TO LEAD. (Ger.) Schwanitz, G. (Inst. Human Genet., U. Erlangen-Nuremberg, Germany), G. Lehnert and E. Gebhart. *Deutsch Med Wschr* 95(32):1636-1641, 1970.

To investigate the correlation between chromosomal damage and occupational exposure to lead, chromosomal analyses and biochemical tests were performed on workers in a lead-oxide factory, where all subjects were found to have a significantly elevated blood lead level (74.7 $\mu\text{g}/100\text{ ml}$ vs normal value of 14.9 $\mu\text{g}/100\text{ ml}$). Blood lymphocyte cultures showed an increased proportion of mitoses with secondary chromosomal aberrations in the workers exposed to lead-oxide, compared with a control group of healthy blood donors. The percentage of abnormal mitoses rose with an increasing δ -aminolevulinic-acid excretion in the urine. In addition to chromosomal breaks there were also nonspecific changes such as spiralizing defects, chromosomal adhesions and pulverization. The proportion of tetraploid mitoses and the mitoses index were slightly increased over those in the control group. *In vitro* experiments with lead acetate solution (10^{-4} to 10^{-6} M) confirmed the abnormalities found in the lead workers. The proportion of abnormal mitoses was largely independent of the added lead acetate concentration.

- 0113 NASAL CANCER IN WOODWORKERS. (E.) Anonymous. *Lancet* 2(7666):253, 1970.

A high correlation between nasal cancer and wood-working was found among woodworkers in the furniture industry in England (29 of 35 patients in one study were woodworkers). Adenocarcinomas, usually originating in the ethmoid sinus, were especially common. Early presenting symptoms included unilateral blood-stained nasal discharge and unilateral nasal obstruction. Wood dust apparently becomes deposited in 2 areas anteriorly on the nasal septum and on the anterior part of the middle turbinate, a frequent site of squamous metaplasia. Prolonged contact of wood dust, which probably contains a carcinogen, with the mucous membrane in the middle turbinate may stimulate tumor formation.

- 0114 CARCINOMA OF THE PENIS INVOLVING SKIN OF BASE. (E.) Grabstald, H. (Mem. Hosp. New York, N.Y.). *J Urol* 104(3):438-440, 1970.

A case of rare skin cancer affecting the base of the penis and diagnosed as low-grade squamous cell carcinoma of the penis is presented. The lesion was noted in a house painter exposed to paints and paint removers for more than 40 yr. A wide local

excision of the tumor which included virtually all of the skin of the penis was done. Radical groin dissection was not carried out. The patient has been free of disease for more than 3 yr postoperatively. Whether the patient's occupation was related to the tumor is not clear.

- 0115 A STUDY OF MORTALITY, SYMPTOMS, AND RESPIRATORY FUNCTION IN HUMANS OCCUPATIONALLY EXPOSED TO OIL MIST. (E.) Ely, T. S. (Lab. Indust. Med., Eastman Kodak Co., Rochester, N.Y.), S. F. Pedley, F. T. Hearne and W. T. Stille. *J Occup Med* 12(7):253-261, 1970.

The incidence of malignant and benign neoplasms was assessed in a study of people occupationally exposed to oil mist concentrations in machine shop environments. Measures of forced vital capacity and one second forced expiratory volume were compared in unexposed control groups and in exposed test groups. The significant predictors of forced vital capacity and forced expiratory volume for the groups studied were consistently height, age, and cigarette years. The symptoms in general yielded the smoking variables, as well as disease history in some cases, as the significant predictors. After the effect of these predictors had been taken into account, the effect of oil-mist exposure or any other job environment, as measured by the number of years on that job, was found to be not significant. Practical machine shop oil mist concentrations experienced by the experimental group were not associated with an increase in any respiratory symptom, including carcinoma-related symptoms.

- 0116 CARCINOMA OF THE SCROTUM. (E.) Milne, J. E. H. (Dept. Hlth., Victoria, Australia). *Med J Aust* 57(1):13-16, 1970.

Five cases of carcinoma of the scrotum were followed up to determine if occupational factors figured in the etiology of the disease. All cases occurred during or after the seventh decade of life (67-88 yr). In 4 of the 5 cases, the subjects had been continuously exposed to oil and grease in the course of their working lives in machine shops, railroad yards and coal mines, following the general pattern of scrotal cancer observed in larger studies. Use of protective outer clothing and personal hygiene, especially skin cleansing, can lower the risk of exposure to those who work with carcinogenic oils.

- 0117 WORKMEN'S SERIAL EXAMINATION FOR CANCER OF THE LARYNX. (Hung.) Farago, L. (Dept. of Ear, Nose and Throat, Nat. Inst. of Oncology, Budapest, Hungary). *Magyar Onkol* 14(2):97-104, 1970.

- 0118 SIGNIFICANCE OF HORMONAL FACTORS IN INDUCING MELANOMA IN HAMSTERS WITH DMBA. (E.) Raitschew, R. (Cancer Inst. Sofia, Bulgaria). *Z Krebsforsch* 74(2):115-121, 1970.

19 EFFECTS OF PHENOBARBITAL, PHENYLBUTAZONE,
3,4-BENZPYRENE, OR 3-METHYLCHOLANTHRENE
ON ETHANOL METABOLISM IN THE RAT. (E.) Reinhard,
F. (Grad. Sch. Pharm. Sci., Northeastern U.,
Boston, Mass.) and E. Spector. *Toxic Appl Pharmacol*
1(1):12-22, 1970.

20 VAGINAL CYTOLOGY IN A STUDY OF CUMULATIVE
EFFECTS OF AN ORAL CONTRACEPTIVE: ACID
MUCOPOLYSACCHARIDE AND KERATIN AS INDICATORS FOR CYCLE
PHASES. (E.) Stern, E. (Sch. Publ. Hlth., U.
California, Los Angeles) and M. R. Mickey. *Acta Cytol*
7(7):382-385, 1970.

21 SEVERE BLOOD DISEASES: INCIDENCE OF EX-
POSURE TO BENZENE. (Fr.) Girard, R. (Hosp.
Guoard Herriot, Lyon, France) and L. Revol. *Nouv*
Rev Franc Hemat 10(4):477-484, 1970.

0122 EFFECT OF SILICON DUST ON THE INCIDENCE OF
3,4 BENZPYRENE-INDUCED LUNG TUMORS IN RATS.
(It.) Novelli, A. (Inst. Gen. Path., U. Genoa, Italy),
U. M. Marinari, D. Cottalasso and L. Santi. *Cancro*
22(4):405-422, 1969.

* Rev (0003)(0015)(0017)(0019)
* Viral (0165)
* Immun (0236)(0237)(0238)
* Epid-Biom (0268)(0276)(0280)(0281)
* Misc (0307)(0309)

- 0123 EFFECTS OF SINGLE-DOSE, WHOLE BODY, ^{60}Co GAMMA IRRADIATION ON NUMBER OF CELLS IN DNA SYNTHESIS AND MITOSIS IN THE MOUSE DUODENAL EPITHELIUM. (E.) Leshner, J. (Allegheny Gen. Hosp., Pittsburgh, Pa.) and S. Leshner. *Radiat Res* 43(2):429-438, 1970.

The number of cells in mitosis and in DNA synthesis in the mouse duodenal epithelium after single-dose, whole body ^{60}Co γ -ray exposures (150, 300, 500, 600, 750, and 1000 r) have been studied with crypt squash autoradiographs by injecting ^3H -thymidine (50 μC , i.p.) at various postirradiation intervals. Changes in the number of cells in mitosis and DNA synthesis after irradiation followed a similar pattern at all dose levels but the degree of change increased with increasing dose. Mitosis was completely blocked for 1 hr after exposure at all levels; then a mitotic lag ranging from 1.5 to 10 hr was observed, followed by a mitotic rate which exceeded control values and went through a series of fluctuating highs and lows damping to a near steady-state cell proliferation rate. The number of cells in DNA synthesis decreased after irradiation for an extended period (10-60 hr) and then exceeded the control values before damping to normal. The immediate block of cells in G_1 and G_2 by irradiation was followed by a rapid rise in the number of cells in mitosis and DNA synthesis, after which cell production returned to normal levels.

- 0124 ISCHEMIA OF THE LUNG DUE TO IONIZING RADIATION: QUANTITATIVE STUDIES. (E.)

Johnson, P.M. (Coll. Phys. Surg., Columbia U., New York, N. Y.), R. H. Sagerman and C. S. Dombrowski. *J Nucl Med* 11(8):491-495, 1970.

Adult female mice were exposed to ionizing irradiation of the right lung in doses ranging from 100-4,000 rads to determine the incidence and severity of pulmonary ischemia consequent to irradiation. Pulmonary blood flow was reduced following radiation; the intensity of radiation-induced pulmonary ischemia was affected by the size of the radiation dose and the length of survival following treatment. During survival periods extending to half the life span of the animal, no evidence could be found of a limiting process or of recovery from radiation-induced pulmonary ischemia.

- 0125 ATYPICAL CHANGES IN THYROID FOLLICULAR CELLS SECONDARY TO RADIOIODINE. (E.)

Murphy, E. (Nat'l. Comm. Nucl. Med., Mexico City, Mexico) and Q. F. B. C. Cervantes. *Amer J Roentgen* 109(4):724-728, 1970.

Rats were injected with 150-700 μC radioiodine 131 to test whether this agent causes atypical cellular changes in thyroid follicles connected with neoplasia. High doses of radioiodine 131 produced marked follicular atrophy with moderate and irregular nuclear enlargement and few mitotic forms. Rats injected with 0.4-2.5 U thyroid stimulating hormone in association with radioiodine revealed microscopic cellular alterations of greater importance than those revealed by rats which did not receive thyroid stimulating hormone.

- 0126 PAPILLARY ADENOCARCINOMA OF THE THYROID DEVELOPING AFTER TREATMENT OF HYPERTHYROIDISM WITH ^{131}I . (E.) Araki, M. (Res. Inst. Nucl. Med. Biol., Hiroshima U., Japan) and K. Oshiro. *Gann* 61(3):267-269, 1970.

A case of papillary carcinoma developing in the thyroid of a Japanese woman, 6 yr after ^{131}I treatment for hyperthyroidism, is reported. The resected tumor was 1.8 x 1.2 x 0.6 cm and surrounded by a capsule composed of concentric layers of collagenous connective tissue. The lesion was well-differentiated, admixed with irregular islands of hyaline connective tissue; the individual cells were small, with distinct vesicular nuclei surrounded by scant eosinophilic cytoplasm. Scattered foci of calcification were present and mitotic figures were rare. The surrounding thyroid tissue was characterized by irregular interstitial fibrosis, consistent with late irradiation changes.

- 0127 WHOLE BODY IRRADIATION OF THE RAT: LATE PULMONARY LESIONS. I. HISTOCHEMICAL STUDIES. (Fr.) Caulet, T. (Fac. Med. Reims, France), J. J. Adnet, M. Pluot and G. Legeay. *Path Europ* 5(2):164-178, 1970.

Histological and histochemical alterations in Wistar rat lungs (88 animals) following whole body irradiation (single exposure, ranging from 100-800 rad) were studied 2-13 months after exposure. Slight sclerotic lesions were noticed sporadically in animals exposed to 400 rad. Collagenous interstitial fibrosis occurred 3-4 months after 500-600 rad exposures; such fibrosis appeared most severe in the lungs of animals exposed to 600, 700 and 800 rad. The interalveolar wall appeared thickened and lined with membranous and granular (phospholipid inclusions) pneumocytes. Emphysema associated sclerotic lesions occurred in animals injected intratracheally with homologous heparinized blood, before or after irradiation; such lesions were characteristically seen 5-12 months after exposure to 500 or 600 rad. Of the hydrolases, acid phosphatase levels increased within the endoalveolar cells and alkaline phosphatases increased within the granular pneumocytes; ATP-ases and 5-nucleotidases increased in areas of hypertrophic reticular pneumonia while esterases increased throughout the cell system. The dehydrogenases increased in all cell types except in the areas of reticular atrophic pneumonia; lactic and glucose-6-phosphate dehydrogenases appeared most elevated, indicating intense local oxidative processes, probably due to the operation of repair mechanisms.

- 0128 WHOLE BODY IRRADIATION OF THE RAT: LATE PULMONARY LESIONS. II. MORPHOLOGY AND CYTOCHEMISTRY, AN ELECTRON MICROSCOPY STUDY. (Fr.) Adnet, J. J. (Fac. Med. Reims, France), T. Caulet, G. Legeay, C. Hopfner and J. L. Guenet. *Path Europ* 5(2):179-197, 1970.

Morphological and cytochemical alterations of lung ultrastructure (alveolar wall and cell lining) were studied in 40 Wistar rats 8 weeks to 11 months following whole body irradiation (single exposure to

levels ranging from 100-800 rad). An additional 21 rats were injected intratracheally with homologous parinized blood in order to study whole body radiation effects on modified lung parenchyma. Minor lesions induced by 100-400 rad levels consisted of slight collagenous scleroses of the alveolar wall, occurring during the second month after exposure. Major lesions, produced by 500-800 rad, consisted of severe fibrosis of the alveolar wall, associated with the occurrence of considerable numbers of mastocytes, dilatation of wall capillaries and an increase of the amount of granular pneumocytes. The blood-treated rats (exposed to 100-800 rad) developed sclerotic emphysema. Acid phosphatases occurred at the lamellar level of granular pneumocytes in cytolytic areas induced by irradiation; alkaline phosphatases were present around the lung capillaries in sclerotic areas above the 600 rad level of exposure, indicating severe circulatory alterations. Dehydrogenases disappeared in the regions of altered granular pneumocytes. Labeled glycine incorporation occurred normally in unaltered granular pneumocytes up to 800 rad levels of exposure, but failed to occur in altered pneumocytes.

29 PROTECTION BY CYSTEAMINE AGAINST MITOTIC DELAY AND CHROMOSOMAL ABERRATIONS INDUCED BY X-RAYS IN SYNCHRONIZED CHINESE HAMSTER CELLS. (E.) C. K. (Argonne Natl. Lab., Ill.) and W. K. Sinclair. *Radiat Res* 43(2):357-371, 1970.

The protective effect of cysteamine (50 mM) on mitotic delay and chromosomal aberration frequency induced by X-irradiation was studied at different stages of the cell cycle in Chinese hamster lung cells (79-S171). Cells not treated with cysteamine and irradiated (625 r) during the S phase showed greater mitotic delay (3-4 hr) than those irradiated in G₁ and (2 hr); cells not irradiated but treated with cysteamine showed delay (1 hr) when treated during the early S and a small delay (30 min) when treated in late S or G₁. Treatment of cells with both irradiation (1500 r) and cysteamine produced a pattern similar to that of cells irradiated without cysteamine except that the required irradiation dose was 2.4 times higher. The dose-modifying factor for mitotic delay was approximately 2.5 throughout the cell cycle. Data on chromosomal aberrations in irradiated (3000 r) cells in the presence of cysteamine indicate that the frequency of aberrations and their distribution were similar to those observed without cysteamine except that the required dose was more than 5 times higher. The dose-modifying factor for aberrations resulting from one hit is approximately 8, and 5.3 for two-hit aberrations.

30 PHILADELPHIA CHROMOSOME IN ACUTE LYMPHOCYTIC LEUKEMIA. (E.) Propp, S. (Albany Med. Coll., Union U., New York) and F. A. Luzzi. *Blood* 36(3):353-360, 1970.

A case of acute lymphocytic leukemia associated with a high percentage of Philadelphia chromosome in the marrow cells is presented. The patient was a roent-

genologist who had been practicing diagnostic radiology, including fluoroscopy, for 11 yr preceding his final illness. Repeated exposure to X-ray irradiation may have caused chromosome damage resulting in the occurrence of the Philadelphia anomaly in lymphocytic leukemia in his case. No Philadelphia chromosome was observed in a 72-hr blood culture using phytohemagglutinin in 50 metaphases counted, which ruled against a congenital defect. The specificity of the Philadelphia chromosome for myeloproliferative disorders should be reconsidered.

0131 ORIGIN OF UNDIFFERENTIATED NEOPLASM FROM VERRUCOUS EPIDERMAL CARCINOMA OF ORAL CAVITY FOLLOWING IRRADIATION. (E.) Kosek, J. C. (VA Hosp., Palo Alto, Calif.), S. D. Proffitt and T. R. Spooner. *Cancer* 26(2):389-393, 1970.

A case is presented of a 61-yr-old man bearing a verrucous carcinoma of the oral cavity which appeared to have undergone anaplastic transformation, an unusual finding in carcinomas of this type. The carcinoma had been treated by X-irradiation. The anaplastic lesion had definite epidermoid differentiation in the form of tonofibrils and tonofilaments, demonstrable only with electron microscopy. It co-existed discretely with the well-differentiated tumor and metastasized independently. Probably, the former lesion arose, not through a transformative dedifferentiation, but as a new carcinoma from the cells of the latter lesion.

0132 POSTIRRADIATION SARCOMA: INCLUDING 5 CASES AFTER X-RAY THERAPY OF BREAST CARCINOMA. (E.) Hatfield, P.M. (Massachusetts Gen. Hosp., Boston) and M. D. Schulz. *Radiology* 96(3):593-602, 1970.

Postirradiation sarcoma was exhibited by 11 patients in a 15-yr survey at Massachusetts General Hospital; sarcomas in such sites as the shoulder, chest, and pelvis, occurred after radiation treatment of primary carcinoma of the breast in 5 cases, and after megavoltage therapy in 3 cases. Because these lesions developed, on an average of about 8 yr after therapeutic exposure to radiation, it is probable that they were caused by radiation and were not examples of the "double primary" phenomenon or of spontaneously occurring osteogenic sarcoma. The frequency of post-irradiation sarcoma of bone in 10-yr survivors of radiation treatment for carcinoma of the breast is estimated to be about 1 post-irradiation sarcoma for every 450 radiation-treated and cured breast carcinomas.

0133 RADIATION-INDUCED SARCOMA AFTER TREATMENT OF BREAST CANCER. (E.) Senyszyn, J. J. (Columbia-Presbyterian Med. Ctr., New York, N. Y.), A. D. Johnson, H. W. Jacox and F. C. H. Chu. *Cancer* 26(2):394-403, 1970.

Radiation-induced sarcomas after treatment of breast carcinoma is reported in 2 patients 23 yr and 7 yr after radiotherapy. An undifferentiated sarcoma of the scapula believed to be induced by a calcu-

lated dose to the soft tissue component of bone of 8,195 rads in 3 weeks was found in one patient. The second patient had a fibrosarcoma involving the soft tissues of the axilla. Both patients died several months after diagnosis of the second neoplasm.

- 0134 ECCRINE POROMA: TWO UNUSUAL VARIANTS. (E.) Penneys, N. S. (U. Miami Sch. Med., Florida), A. B. Ackerman, S. N. Indgin and S. H. Mandy. *Brit J Derm* 82(6):613-615, 1970.

Two cases of eccrine poroma are described which were regarded as atypical in that one affected the nose, and one occurred in an area of radiation-altered skin. In Case 1, in the region of chronic radiodermatitis in which the eccrine poroma originated, akinetic keratosis, squamous cell carcinomas and an atypical fibroxanthoma had developed. The irradiated area had been affected previously with several cutaneous malignancies; the other hand had been affected by numerous tumors, including atypical fibroxanthoma, squamous cell carcinomas, Bowen's disease, and several keratoses. An unusual feature of the eccrine poroma in Case 2 was the presence of numerous mitotic figures.

- 0135 MALIGNANT ADENOMA OF THE THYROID OCCURRING AFTER ROENTGEN THERAPY IN CHILDHOOD. (Ger.) Gilly, L. (Recklinghausen Inst. Radiol., Germany) and D. Meese. *Strahlentherapie* 139(6):695-697, 1970.

An 18-yr-old male developed a malignant papillary adenoma of the thyroid 15 yr after roentgen therapy (a total of 260 rad) for bilateral cervical lymph nodes. Thyroidectomy followed by cobalt therapy led to complete recovery of the patient. Similar cases on large patient populations (minimal dose of radiation received at least 180 rad) are reviewed.

- 0136 IRRADIATION GASTRITIS SIMULATING CARCINOMA. (E.) Lane, D. (Mater Hosp., Brisbane, Australia). *Med J Aust* 57(13):576-577, 1970.

Two cases are presented in which standard deep X-ray therapy was given after nephrectomy for carcinoma of the kidney; the patients' stomachs in both cases had the radiological appearance of carcinoma, the diagnostic choice being between carcinoma of the stomach and chronic gastritis. In the first case, although there was no gastroscopic evidence of cancer, the patient finally died of metastasizing tumors in the lumbar spine, while in the second case, the final diagnosis was fibrosis secondary to X-ray treatment.

- 0137 CLINICAL, HISTOCHEMICAL AND CYTOGENETIC FINDINGS IN PATIENTS WITH THOROTRAST DAMAGE. (Ger.) Hennekeuser, H. H. (2nd Med. U. Clin. Mainz, Germany), P. Citoler, H. Niemczyk and A. Gropp. *Klin Wschr* 48(15):895-906, 1970.

Clinical, histological and cytogenetic investigations in 6 men and 3 women (40-66-yr-old), who had angio-

graphy with thorotrast 19-28 yr before, revealed 1 patient with lymphosarcoma, 3 patients with local granulomas (at the site of contrast medium injection) and 5 patients with enlarged livers. Lymphocyte cultures from the peripheral blood of all 9 patients had abnormal chromosomes while no chromosomal aberrations were detected in the bone marrow cells (thorotrast positive) of 4 examined patients. Liver needle biopsies in 6 patients revealed the presence of thorotrast, detectable by microscopy and autoradiography. Only 2 patients had fibrosis of the liver.

- 0138 TREATMENT OF RADIATION-INDUCED NODULAR GOITERS. (E.) De Papp, Z. G. (U. Rochester Sch. Med., Dent., N. Y.), R. A. Pincus and L. H. Hemplemann. *J Nucl Med* 11(8):496-502, 1970.

- 0139 COMBINED DAMAGE STUDIES. WHOLE BODY IRRADIATION AND SURGICAL SKIN LESIONS IN RATS: VARIATIONS OF HISTAMINE LEVELS IN DIFFERENT ORGANS. (Ger.) Messerschmidt, O. (Radiol. Inst. U. Freiburg, Germany), V. Seydewitz and L. Koslowski. *Strahlentherapie* 139(6):724-734, 1970.

- 0140 PRIMARY CANCER OF THE GASTRIC STUMP AFTER GASTRECTOMY FOR ULCER DISEASE. (Fr.) Stanciu, G. (Tirgu-Mures, Rumania). *J Radiol Electr* 51(6-7):379-384, 1970.

- * Rev (0001)(0016)
- * Chem (0040)(0044)(0046)(0068)
- * Viral (0211)
- * Immun (0225)
- * Misc (0307)

- 41 DNA-DIRECTED DNA POLYMERASE ACTIVITY IN ONCOGENIC RNA VIRUSES. (E.) Spiegelman, (Inst. Cancer Res., Columbia U., New York, N. Y.), Burny, M. R. Das, J. Keydar, J. Schlom, M. Travnicek and K. Watson. *Nature* 227(5262):1029-1031, 1970.

DNA-directed DNA polymerase has been detected in 6 oncogenic RNA viruses (Rauscher leukemia, Rous sarcoma, avian myeloblastosis, murine mammary tumor, Moloney sarcoma and feline leukemia viruses). DNA synthesis with all 4-deoxyriboside triphosphates, Mg^{+2} and DNA was monitored by incorporation of 3H -dATP; the viral preparations used were pretreated with micrococcal nuclease to eliminate the viral RNA. The identity of the product of the reaction was confirmed by its sensitivity to deoxyribonuclease and equilibrium density centrifugation. The response of the avian myeloblastosis viral DNA-RNA polymerase to different DNA templates (CEF, MEF, *E. coli* and T6) revealed that the oncogenic viral DNA polymerase preferred double to single stranded DNA. The results of hybridizing each of 3 DNA products to 3 DNA templates (mouse, *E. coli* and T6) showed that hybridizability of each product was much superior when challenged with the DNA actually used in its synthesis. These data suggest that the DNA polymerase of the oncogenic viruses is not copying random segments of these vertebrate DNA's.

- 42 CHARACTERIZATION OF THE PRODUCTS OF RNA-DIRECTED DNA POLYMERASES IN ONCOGENIC RNA VIRUSES. (E.) Spiegelman, S. (Inst. Cancer Res., Columbia U., New York, N. Y.), A. Burny, M. R. Das, J. Keydar, J. Schlom, M. Travnicek and K. Watson. *Nature* 227(5258):563-567, 1970.

Given tumor viruses (Rauscher murine leukemia, Moloney sarcoma, mammary tumor, feline leukemia, avian myeloblastosis, monkey mammary tumor and Rous sarcoma viruses) were purified and the incorporation of 3H -TTP into an acid-insoluble product was followed with each virus. The acid-insoluble product, after isolation and purification, could be degraded by deoxyribonuclease but not by ribonuclease, pronase or NaOH. Equilibrium density centrifugation and base frequency analysis established that the product was a DNA heteropolymer. The outcome of an annealing reaction between the DNA synthesized by Rauscher leukemia virus polymerase and excess RNA purified from the same virus resulted in complete hybridization. The specific complementarity of the DNA product to the viral RNA and the occurrence of DNA-RNA hybrids in the course of the reaction seem to establish the existence of RNA-directed DNA polymerases in the oncogenic viruses.

- 43 FORMATION OF VIRAL RNA-DNA HYBRID MOLECULES BY THE DNA POLYMERASE OF SARCOMA-LEUKEMIA VIRUSES. (E.) Rokutanda, M. (St. Louis U. Sch. Med., Mo.), H. Rokutanda, M. Green, K. Fujinaga, K. Ray and C. Gurgo. *Nature* 227(5262):1026-1028, 1970.

Evidence that the template for the DNA polymerase of the sarcoma-leukemia viruses is viral RNA is presented. ^{32}P -labeled viral RNA was used in the standard DNA polymerase assay with 3H -TTP; after 90 min, both labels

cosedimented at 70 S. Treatment with pronase and Cs_2SO_4 density gradient analysis indicated hybrid formation had occurred. Alkaline hydrolysis resulted in the release of 3H -DNA; incubation of viral ^{32}P -RNA and 3H -DNA in annealing conditions converted the DNA to a hybrid. The viral RNA-DNA hybrid is probably the initial product of the virus DNA polymerase reaction, since only small amounts of free product were found even after 90 min of reaction.

- 0144 TUMOR-INDUCED SKIN HETEROGENIZATION: II. VIRUS CAUSING THE PHENOMENON. (E.) Svet-Moldavsky, G. (Inst. Exp. Clin. Oncol., Moscow, USSR), A. L. Liozner, D. M. Mkheidze, P. P. Sokolov and A. P. Bykovsky. *J Nat Cancer Inst* 45(3):475-484, 1970.

A permanent skin-heterogenizing virus was contained in sarcoma K-237 of C57BL/6J mice; the virus was ether resistant, thermolabile and could be specifically neutralized with C57BL/6J immune serum. It caused the same phenomenon of tissue incompatibility as the tumor itself. Preliminary sedimentation data which showed the virus particles to be very small was confirmed partly by the discovery of two types of virions, 175 and 80 A in diameter, in an active fraction of the homogenate. Homogenates obtained from tumors of the 7th-22d passages contained skin-heterogenizing virus titers of 10^8 - 10^{12} heterogenization-producing doses/ml, but those obtained from tumors of the 23d-27th passages contained 10^1 - 10^5 . The state of heterogenization was maintained in infected mice from the 21st-240th day after inoculation. The behavior patterns of the virus in tumor cells were somewhat different from those of skin grafts. Apparently, the virus in the skin is in some way integrated with the cells and passes from cell to cell by some unknown mechanism. Infectious virus was obtained from the skin homogenate only once after inoculation with tumor homogenate but never after skin graft infection. Nevertheless, each skin passage resulted in skin heterogenization. Skin-heterogenizing virus persisted in the spleen of rejector mice in large amounts (titers 10^5 - 10^7) at least for 120 days after infecting grafting. The exchange skin grafting between rejector mice resulted in survival of transplants, though the skin from the same animals was rejected as usual by normal C57BL/6J recipients.

- 0145 TUMOR-INDUCED SKIN HETEROGENIZATION: III. IMMUNOLOGIC AND IMMUNOGENETIC MECHANISMS. (E.) Liozner, A. L. (USSR Min. Hlth., Moscow), G. J. Svet-Moldavsky and D. M. Mkheidze. *J Nat Cancer Inst* 45(3):485-494, 1970.

Mice from 4 different strains were inoculated with K-237 sarcoma, given skin grafts from tumor-bearing donors and injected with cell-free tumor homogenate to determine whether the strain specificity of skin heterogenizing virus obtained from K-237 sarcoma was determined by the generic constitution of the animals. Skin heterogenizing virus produced syngeneic skin rejection in C57BL/6J mice inoculated with any type of virus-containing materials, i.e., tumors, skin grafts, or cell-free tumor homogenates, but had no effect on BALB/c, CBA, C3HA, C3Hf, and T6T6 mice. Hybrid mice

(C57BL/6J X BALB/c) F_1 also resisted the heterogenizing action of the virus,¹ despite the fact that K-237 sarcoma always grew progressively in these hosts. Sensitivity to heterogenizing virus action seemed to be controlled by a recessive gene (or genes), and the C57BL/6J strain was probably homozygous in respect to the hypothetical gene. F_2 hybrid mice appeared to be somewhat sensitive to the heterogenizing action of the virus. Furthermore, some sensitive F_2 mice acquired the ability to infect C57BL/6J mice with skin heterogenizing virus as a result of skin grafting. Various immunosuppressive treatments such as whole-body γ -irradiation or cyclophosphamide not only delayed rejection of heterogenized skin but often abolished it. Far from being accelerated, the rejection of secondary grafts of C57BL/6J heterogenized skin was delayed 2-4 days. However, the second-set rejection of C57BL/6J heterogenized skin occurred after it was transplanted to (C57BL/6J X BALB/c) F_1 mice sensitized with similar grafts 3 weeks before. K-237 sarcoma cells failed to produce the new transplantation antigen present in skin cells, although the latter did not provide mature virus reproduction. These contradictory results may be due to the specificity of the viruses studied.

- 0146 A NEW VIRUS IN A SPONTANEOUS MAMMARY TUMOR OF A RHESUS MONKEY. (E.) Chopra, H. C. (John L. Smith Mem. Cancer Res., Charles Pfizer Co., Maywood, N. J.) and M. M. Mason. *Cancer Res* 30(8): 2081-2086, 1970.

Electron microscopy of a spontaneous mammary tumor developed by a female rhesus monkey was performed to investigate the ultrastructure and development of virus particles found in the tumor. Thin-section electron microscopy of the tumor tissue revealed 2 types of particles, an intracytoplasmic, electron-dense, ring-shaped particle measuring about 70 m μ in diameter and which occurred singly or in clusters; the density of the viral material was usually higher in the periphery, giving the particle a doughnut-shaped appearance. The other type was an extracellular particle with an outer unit membrane and a central dense nucleoid measuring about 110 m μ in diameter. The intracytoplasmic development and virus maturation by a process of budding at the level of the cell membrane was reconstructed from the electron micrographs. Although the identification of virus particles in monkey mammary carcinoma does not prove an etiological connection between the particles and the tumor, these particles distinctly resemble oncogenic RNA-type virus particles.

- 0147 IMMUNOLOGIC STUDIES OF HUMAN SARCOMAS: ADDITIONAL EVIDENCE SUGGESTING AN ASSOCIATED SARCOMA VIRUS. (E.) Eilber, F. R. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.) and D. L. Morton. *Cancer* 26(3):588-596, 1970.

The incidence of antibody to sarcoma-specific antigens prepared from human liposarcoma in the serum of patients with skeletal and soft tissue sarcoma was subjected to immunological study. Antigen prepared from SA-1 liposarcoma cells with titers of 1/8-1/64 reacted with 9 out of 10 sarcoma sera, while antigen with a titer 1/4 reacted with 1 out of 4

normal sera. The sarcoma-specific antigen was found in tissue culture cells derived from different histologic types of sarcoma but not in normal fibroblasts obtained from sarcoma patients, nor in cells from nonsarcomatous malignancies. Evidence for a relationship between the sarcoma antigen and an infectious agent included the observation that the antigen was common to different sarcomas, and the finding of a high incidence of antibody to the sarcoma antigen in close family members of the sarcoma patients. This relationship was confirmed by the demonstration that cell-free extracts derived from sarcoma tumors and filtered extracts from sarcomas in tissue cultures were capable of inducing the formation of the sarcoma-specific antigen in normal human cells. Evidently, there exists a filterable agent in human sarcomas capable of inducing a new sarcoma-specific antigen on normal human cells in tissue culture.

- 0148 RIBONUCLEIC ACID TRANSCRIPTASE ACTIVITY IN PURIFIED WOUND TUMOR VIRUS. (E.) Black, D. A. (Dept. Molec. Biol., U. California, Berkeley) and C. A. Knight. *J Virol* 6(2):194-198, 1970.

Wound tumor virus was isolated from infected sweet clover root tumors and subjected to standard polymerase activity assays in order to characterize an associated RNA transcriptase possessed by cells in this tumor. The product of transcriptase synthesis was found to be single-stranded RNA which annealed specifically to wound tumor viral RNA. Studies with RNA of cytoplasmic polyhedrosis virus, which also contains an associated RNA transcriptase, showed no common relationship between the two RNAs.

- 0149 VIRUS-LIKE PARTICLES IN LEUKEMIA CELLS OF A NEWBORN: ELECTRON MICROSCOPIC COMPARISON WITH HERPES SIMPLEX VIRUS. (Ger.) Lamper, F. (Child. Clin. U. Munich, Germany). *Klin Wschr* 48(12): 737-741, 1970.

Virus-like particles were detected in bone marrow leukemic cells of a 4-month-old female infant (post mortem) and compared to similar particles in a herpes simplex virus-infected cell culture. High resolution electron microscopy of these particles revealed 3 kinds of virus-like formations similar to those occurring at various maturation stages of the herpes simplex virus; these particles included vacuolated hexagonal naked "capsid" nucleocapsids (with an electron dense nucleus), and nucleus-like formations lacking the external capsid protection in portions where broken chromatin strands occurred. Nucleus-like formations were more frequent and capsid particles were less frequent in leukemic cell particles than in herpes virus simplex. The average capsid diameter of the leukemic cell virus particles was 1240 A and 1017 A in case of the herpes simplex virus capsid. The average nucleocapsid dry matter content, determined by quantitative electron microscopy, was 19.4×10^{-6} g for the leukemic cell particles and 7.6×10^{-6} g for the herpes simplex virus.

- 0150 LEUKEMIA IN FANCONI'S ANEMIA: CYTOGENETIC AND TUMOR VIRUS SUSCEPTIBILITY STUDIES. (E.) Dosik, H. (Maimonides Med. Ctr.,

Brooklyn, N.Y.), L. Y. Hsu, G. J. Todario, S. L. e, K. Hirschhorn, E. S. Selirio and A. A. Alter. *Proc Natl Acad Sci USA* 66(3):341-352, 1970.

family with 2 male children affected with Fanconi's anemia is described; 1 child developed acute myelomonocytic leukemia, an established concomitant of Fanconi's anemia, an inherited disorder characterized by multiple congenital abnormalities, chromosome anomalies and irreversible aplastic anemia. Chromosome preparations in both parents showed abnormalities, a previously unreported finding. Fibroblast cultures from both parents and one brother inoculated with simian virus 40 developed increased numbers of transformed colonies, compared with normal control cultures similarly inoculated. The presence of chromosome abnormalities and cellular susceptibility to oncogenic agents appear to be related to an increased risk of malignancy.

51 SEROEPIDEMIOLOGICAL STUDIES ON NASOPHARYNGEAL CARCINOMA BY FLUORESCENT ANTIBODY TECHNIQUES WITH CULTURED BURKITT LYMPHOMA CELL. (E.) Kawamura, A., Jr. (Inst. Med. Sci., U. Tokyo, Japan), M. Takada, A. Gotoh, K. Hamajima, T. Sanpe, T. Murata, Y. Ito, T. Takahashi, T. Yoshida, T. Hayama, S. M. Tu, C. H. Liu, C. S. Yang and C. H. Ng. *Gann* 61(1):55-71, 1970.

Examination of the sera of Burkitt lymphoma patients and nasopharyngeal carcinoma patients from Japan and Taiwan by a standardized method for detecting anti-Epstein-Barr virus antibodies showed that antibody titers of Chinese patients were higher than those of Japanese subjects. Furthermore, ridit analysis revealed that sera from infectious mononucleosis patients exhibited higher titers than those of leukemia, other cancers, and normal subjects; however, these titers were lower than those of the nasopharyngeal carcinoma and Burkitt lymphoma. Anti-EB virus titer higher than 1:640 was found in the sera of 85.7% of Burkitt lymphoma patients (7 cases), 91.1% of Chinese nasopharyngeal carcinoma patients (8 cases) in Taiwan, and 63.6% of Japanese nasopharyngeal carcinoma patients (11 cases), as compared with 15% in other malignancies and 5-15% in normal subjects. The sera of both nasopharyngeal carcinoma and Burkitt lymphoma patients appear to contain antibodies which possess the same or quite similar reactivity against the Epstein-Barr virus.

52 BURKITT'S TUMOR IN A TEN YEAR OLD BOY CONFIRMED HISTOLOGICALLY AND VIROLOGICALLY. (E.) Goetz, O. (Path. Inst. U. Munich, Germany), Lampert, P. Peller and K. Prechtel. *Munchen Med Wochenschr* 112(30):1373-1376, 1970.

The first case report of juvenile Burkitt's lymphoma in Germany, a 10-yr-old boy, is presented. The tumor was histologically assessed as a lymphosarcoma. Epstein-Barr viruses in tumor tissue culture and antibodies against Epstein-Barr virus, which developed during the course of the disease, were demonstrated by immunofluorescence.

0153 REACTIVITY OF RADIOIODINATED SERUM ANTIBODY FROM BURKITT'S LYMPHOMA AND NASOPHARYNGEAL CARCINOMA PATIENTS AGAINST CULTURE LINES DERIVED FROM BURKITT'S LYMPHOMA. (E.) Inoue, M. (Karolinska Inst., Stockholm, Sweden) and G. Klein. *Clin Exp Immun* 7(1):39-50, 1970.

Cells from Burkitt lymphoma lines, 1 line carrying Epstein-Barr virus and 1 line virus-free, were exposed to radioiodinated conjugates of the IgG serum immunoglobulin fractions of 2 Burkitt lymphoma and 1 African nasopharyngeal carcinoma patients. All 3 radioiodinated conjugates attached to live cells of an Epstein-Barr virus-carrying Burkitt line, but not to Epstein-Barr virus-free cells. A Swedish control serum did not block the binding of any of the 3 conjugates, whereas various unconjugated sera showed various degrees of blocking and cross-blocking. The blocking patterns were in good agreement with previous tests, performed with the same sera against their fluorescein conjugated derivatives. Antibody release tests, involving preincubation of live cells with one of the 3 conjugates, followed by incubation with unlabeled serum revealed a certain hierarchy between the 3 sera with regard to their ability to displace radioiodinated surface-coupled immunoglobulin. This ability could be related to the competitive behaviour of the same sera in the cross blocking tests. The results are believed to reflect differences in the affinity of the 3 antibodies due to differences in the duration of immunization in the 3 patients or to differences in affinity or fit to the surface antigens carried by the Epstein-Barr virus-carrying target cells.

0154 INFECTIOUS MONONUCLEOSIS FOLLOWED BY BURKITT'S TUMOR. (E.) Cohen, M. H. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), Y. Hirshaut, D. Stevens, E. W. Hull, J. W. Davis and P. P. Carbone. *Ann Intern Med* 73(4):591-593, 1970.

Studies were carried out to identify anti-Epstein-Barr virus antibody and Epstein-Barr virus antigen in the serum and bone marrow of a 17-year-old female patient who developed a tumor histologically and cytochemically identical to African Burkitt's tumor 16 months after having had infectious mononucleosis. Antibodies to Epstein-Barr virus were found in the patient. Although Epstein-Barr virus antigen could not be detected in any tissue taken directly from the patient, viral antigen was detected in buffy coat material after establishment in long-term culture. These studies indicate that there is either a different causal agent for these two diseases or that malignant transformation may have occurred during the acute phase of infectious mononucleosis, and the tumor became clinically recognizable 16 months later.

0155 INCIDENCE OF ANTIBODY TO EB VIRUS, HERPES SIMPLEX AND CYTOMEGALOVIRUS IN HODGKIN'S DISEASE. (E.) Aisenberg, A. C. (Massachusetts Gen. Hosp., Boston) and J. M. Goldman. *Cancer* 26(2):327-331, 1970.

The incidence of antibody against EB virus, herpes simplex and cytomegalovirus was measured in 57

patients with Hodgkin's disease and 54 age-matched control subjects. Serum specimens were tested for EB virus antibody using an indirect immunofluorescent technique and for herpes simplex and cytomegalovirus antibodies by a complement fixation method. No differences were seen in antibody titers to all three viral agents between patients with Hodgkin's disease and control subjects (50% with EB virus, 35% with herpes simplex and 7-8% with cytomegalovirus at age 15-34 yr and 30-40% higher for all three agents at age 35-70 yr). None of these viruses appear to play any part in the etiology of Hodgkin's disease. Furthermore, patients with lymphoproliferative disease do not seem to be any more susceptible to EB virus than the normal population.

- 0156 RELATIONSHIP OF EPSTEIN-BARR VIRUS-INDUCED MEMBRANE ANTIGENS IN LYMPHOID CELLS TO VIRAL ENVELOP ANTIGENS. (E.) Gerber, P. (Div. Biol. Standards, Natl. Inst. Hlth., Bethesda, Md.) and G. Goldstein. *J Immunol* 105(3):793-795, 1970.

The nature of immunofluorescent membrane antigens located on the surface of Epstein-Barr virus-infected lymphoma cells was investigated, and compared with antigens on cells derived from Burkitt's lymphoma. The sera from 20 patients with Burkitt's lymphoma or infectious mononucleosis, from normal human donors and chimpanzees were incubated with Raji (Epstein-Barr virus-free), HRIK-P3J from Burkitt's lymphoma (5-50% of cells with immunofluorescent Epstein-Barr virus antigen) or Epstein-Barr virus-transformed human lymphoid cell lines. The Epstein-Barr virus-transformed cells and the HRIK cells reacted only with Epstein-Barr virus-positive sera, 70-80% and 30-50%, resp. Immunofluorescent membrane antigens of Epstein-Barr virus-infected lymphoid cells from a normal donor and from a patient with Burkitt's lymphoma appear to be identical and to contain components of the viral envelop.

- 0157 VIRAL ANTIGEN, VIRUS PARTICLES, AND INFECTIVITY OF TISSUES FROM CHICKENS WITH MAREK'S DISEASE. (E.) Calnek, B. W. (New York State Vetr. Coll., Ithaca, N.Y.), T. Ubertini and H. K. Adldinger. *J Nat Cancer Inst* 45(2):341-351, 1970.

Tissue cultures from chickens which were exposed to Marek's disease herpes virus were subjected to fluorescent antibody and agar-gel precipitin tests and to electron microscopy to investigate their viral particle contents, their viral antigens, and their infectivity; some tissues were also assayed *in vitro* for cellular and cell-free materials. All samples of feather follicle epithelium were positive for antigen detectable by fluorescent antibody and agar-gel precipitin tests, contained large numbers of both naked and enveloped herpesvirus particles, and were the source of infectious, cell-free virus. The bursa of Fabricius, kidney, leukotic gonad, and nerve plexuses also contained fluorescent antibody-detectable antigen but not so consistently or extensively as did the feather follicle epithelium. All these tissues, except kidney, were found positive by the agar-gel precipitin test and were determined by electron microscopy to be infected, but nearly all virus

particles were naked and intranuclear. Infectivity was cell-associated, as shown by *in vitro* virus assays.

- 0158 MAREK'S DISEASE HERPESVIRUS IN PERIPHERAL NERVE LESIONS. (E.) Ubertini, T. (New York State Vetr. Coll., Ithaca) and B. W. Calnek. *J Nat Cancer Inst* 45(3):507-514, 1970.

A chicken experimentally exposed by continuous contact exposure to chickens infected with Marek's disease herpesvirus was autopsied at 34 days with special attention to its sciatic and brachial nerve plexuses. Electron microscopy revealed ultrastructural lesions in both nerves indicating activation of Schwann cells and degeneration of some lymphoid cell elements. Neuronal damage also was observed. The brachial plexus contained Schwann cells, immature lymphoid cells, and degenerated lymphoblastoid cells (Marek's disease cells) with characteristic intranuclear herpesvirus particles. Similar cells in the sciatic plexus appeared to contain no virus particles.

- 0159 PLAQUE TYPES AND CELL-FREE VIRUS FROM TISSUE CULTURES INFECTED WITH CAL-1 STRAIN OF HERPESVIRUS ASSOCIATED WITH MAREK'S DISEASE. (E.) Mikami, T. (Sch. Vetr. Med., U. California, Davis) and R. A. Bankowski. *J Nat Cancer Inst* 45(2):319-333, 1970.

Two distinct plaque types produced with the Cal-1 strain of Marek's disease virus in chicken kidney cell cultures, and the differences in the quantity of free infectious virus produced by each were investigated. The smaller type 1 plaque, normally observed on primary isolation of the agent from chickens infected with Marek's disease, was replaced by a larger type 2 plaque by the fourteenth serial passage. The type 2 plaques grew more rapidly. By the 5th-6th day the plaques were 1.0-2.5 mm in diameter and characterized by pronounced cytoplasmic vacuolation of the affected cells, followed by lysis. Intranuclear inclusions were more frequent in cells of the type 2 plaques than in cells of the type 1 plaques. The addition of 10% dimethylsulfoxide and 10% fetal calf serum to Eagle's basal medium resulted in a marked sparing effect as demonstrated by recovery of infectious virus from chick kidney cell cultures after freezing and thawing, sonic disruption, centrifugation, or vibration. Type 2 plaque-producing virus was recovered from filtrates of supernatants of cell cultures as well as chick kidney cell cultures disrupted by freezing and thawing and passed through a 1.2 μ Millipore membrane. Although fusion of cells appeared to increase recovery of virus which produced the type 1 and type 2 plaques, the yield of Marek's disease virus was not significantly increased in chick kidney cell cultures by the addition of inactivated and concentrated Sendai virus.

- 0160 SUSCEPTIBILITY TO AN AVIAN LEUKOSIS-SARCOMA VIRUS: CLOSE ASSOCIATION WITH AN ERYTHROCYTE ISOANTIGEN. (E.) Crittenden, L. B.

ric. Res. Serv., Beltsville, Md.), W. E. Briles
H. A. Stone. *Science* 169(3952):1324-1325, 1970.

geny embryos of an inbred RPRL strain of chickens
ch is known to be segregating at the gene loci
controlling susceptibility to avian leukosis-sarcoma
us were tested for susceptibility by inoculation
h Rous sarcoma virus and their erythrocytes were
ted for antigens. A dominant gene for suscepti-
ity to infection by avian leukosis-sarcoma virus
shown to be associated with the presence of an
throcyte isoantigen. An isoantigen and a cell
brane receptor for an oncogenic virus may both
controlled by the same gene; alternatively,
sely linked genes or a complex gene locus may
trol both the antigen and viral susceptibility.

1 PERIPHERAL NERVE LESIONS SIMILAR TO THOSE
OF MAREK'S DISEASE IN CHICKENS INOCULATED
H RETICULOENDOTHELIOSIS VIRUS. (E.) Witter, R. L.
gional Poultry Res. Lab., East Lansing, Mich.),
G. Purchase and G. H. Burgoyne. *J Nat Cancer Inst*
3):567-577, 1970.

ite leghorn chickens inoculated with reticuloendo-
liosis virus developed gross lymphoproliferative
ral lesions similar to lesions associated with
ek's disease. Induction of these nerve lesions
reticuloendotheliosis virus stocks from 4 differ-
sources and substantial cross neutralization be-
en neurotropic and viscerotropic reticuloendotel-
is virus stocks were evidence that the lesions
e specific for reticuloendotheliosis virus. Nerve
ions induced by the virus were characterized by
ndant plasma cells, but they could not always be
ferentiated from lesions of Marek's disease. How-
r, the absence of contact spread and the high sus-
tibility of line 6 chickens were some obvious
characteristics distinguishing this syndrome from
t of Marek's disease. No antibody against reticu-
ndotheliosis virus was detected in 5 commercial
cks of chickens with extensive Marek's disease
ses, and evidence was lacking that reticuloendo-
liosis virus infection was of economic importance.

2 LACK OF EFFECT OF BURSECTOMY ON MAREK'S
DISEASE. (E.) Payne, L. N. (Houghton
ltry Res. Station, Huntingdon, England) and M.
nie. *J Nat Cancer Inst* 45(2):387-397, 1970.

born chicks of a Rhode Island Red strain highly
ceptible to Marek's disease and in which the
ease had been induced by Marek's disease herpes-
e virus were bursectomized, with or without total
y X-irradiation, to determine whether this treat-
t would reduce the mortality from Marek's disease.
mortality in infected sham-operated chickens
h and without X-irradiation was 93% and 80%,
p.; the mortality in infected bursectomized chick-
with and without X-irradiation was 100% and 93%,
p. The production of Marek's disease in chickens
h varying degrees of impairment of the bursal
phoid system, including some chickens which ap-
ently lacked antibodies, immunoglobulins, ger-
al centers, and plasma cells, suggested that the
hogenesis of the disease did not depend on the
sa and bursa-dependent lymphoid tissues.

0163 METHODS FOR THE DETECTION OF VIRAL ANTIGEN
AND ANTIBODY TO A FELINE LEUKEMIA VIRUS:
A PRELIMINARY REPORT. (E.) Sibal, L. R. (Natl. Cancer
Inst., Natl. Inst. Hlth., Bethesda, Md.), M. A. Fink,
E. J. Plata, B. E. Kohler, F. Noronha and K.M. Lee.
J Nat Cancer Inst 45(3):607-612, 1970.

Sheep redblood cells coated with virus extracts from
cultured thymus cells from a cat with experimental
leukemia and goat serum from immunized animals were
used in passive hemagglutination-inhibition and micro-
immunodiffusion tests in order to detect and measure
feline leukemia virus antigens in tumor and tissue
extracts. Various tissues from 12 of 13 cats with
spontaneous leukemia (lymphosarcoma) contained feline
leukemia virus antigen; normal cat tissues did not.
The predominant antigen detected in these tests was
an inner component of the virion. None of 20 cat
sera showed antibody to this antigen. However, in
hemagglutination and focus reduction tests antibodies
to an outer coat antigen of the virus were observed
in the serum of some normal and leukemic cats.

0164 FELINE LEUKEMIA VIRUS: PURIFICATION FROM
TISSUE CULTURE FLUIDS. (E.) Burger, C. L.
(St. U. New York Upstate Med. Ctr., Syracuse) and
F. Noronha. *J Nat Cancer Inst* 45(3):499-506, 1970.

A method for the isolation and concentration of large
amounts of leukemia virus from a lymphoid cell line
grown in suspended cell culture, derived from kit-
ten F-422, is reported. After an initial concentra-
tion of tissue culture supernatant by continuous-
flow centrifugation, isopycnic separation was done
on a step gradient of 10, 30 and 60% sucrose
(87,000 x g for 3 hr). The portion showing the
greatest viral concentration appeared at the 1.20
g/cc density level. Each 1.5 l of supernatant from
the cell culture contained approximately 100 µg
nucleic acid in the bands containing the virus.
Reovirus was a contaminant in some cultures used
for separation of the leukemia virus, but the den-
sity of this virus was 1.3 g/cc and easily separated.

0165 ANTIGENIC ANALYSIS OF L STRAIN CELLS: A
NEW MURINE LEUKEMIA-ASSOCIATED ANTIGEN,
"L". (E.) LeClerc, J. C. (Hosp. St. Louis, Paris,
France), J. P. Levy, B. Varet, S. Oppenheim and A.
Senik. *Cancer Res* 30(7):2073-2079, 1970.

Serological analysis of a non-leukemic mouse tissue cul-
ture cell line of the L strain and the induction of
transplantation immunity were performed; 3 antigens as-
sociated with murine leukemia virus were observed in
these healthy cells. The antigens observed included
the group-specific antigen of murine leukemia virus-
es and an antigen common to Friend, Moloney, Rauscher,
and Graffi leukemias. The group-specific and Friend,
Moloney, Rauscher and Graffi antigens are probably
related to the nonleukemogenic type C virus present
in L Cells. A new antigen, L antigen, which is also
present in various virus-induced leukemias of several
strains and in the dimethylbenzanthracene-induced
leukemia was also observed. L antigen was shown to
be different from other already described murine leu-
kemia antigens. No tumor rejection of L+ tumors was

observed in hyperimmune mice despite the presence of cytotoxic antibodies in the blood. Enhancement of tumor growth was frequently observed in this situation. The role of the L antigen in tumor rejection is unclear; it may be that immunization against the L antigen leads to immunological enhancement rather than rejection.

- 0166 MURINE MYELOPROLIFERATIVE VIRUS IN CELL CULTURE. (E.) Soule, H. D. (Michigan Cancer Found., Detroit) and W. J. Arnold. *J Nat Cancer Inst* 45(2):253-262, 1970.

A cell culture system, MCF-6, which was able to maintain for over 2 yr a virulent leukemogenic virus has been isolated from BALB/c mice. The primary culture from which the stable cell line was derived was initiated from pooled lymph nodes combined with the thymus and spleen from a BALB/c mouse with advanced leukemia from inoculation with DICR-5 cell-free supernatant. Cells or supernatant from MCF-6 produced myeloproliferative disorders when injected into neonatal BALB/c mice (but not in older animals) with mortalities of 70-90% after mean latencies of onset of between 100-150 days. Electron micrographs of MCF-6 supernatant showed particles resembling murine leukemia-inducing viruses. Cells from the culture did not transplant, but spleen cells from infected mice were transplantable and produced malignancy in 92% of young adult animals inoculated, with a mean latency of 31 days.

- 0167 LYMPHOSARCOMA: VIRUS-INDUCED THYMIC-INDEPENDENT DISEASE IN MICE. (E.) Abelson, H. T. (Child. Hosp. Med. Ctr., Boston, Mass) and L. S. Rabstein. *Cancer Res* 30(8):2213-2222, 1970.

A lymphosarcoma virus was isolated from a tumor which had developed in a mouse treated with high doses of prednisolone (0.05 mg twice a week for 93 days) and inoculated with Moloney MLV³ leukemia virus at 28 days of age. Mice and rats infected with this lymphosarcoma virus within 36 hr after birth developed solid lymphoid tumors after a latent period of 26-32 days. A unique feature of the induced condition was the lack of thymic involvement; thymic-independent tumor induction distinguishes this virus from the other experimental murine lymphoid leukemia viruses. Massive meningeal tumors, a myelocytic leukemoid reaction, and the absence of evidence of a disseminated leukemia were features of this disease.

- 0168 PROLIFERATIVE ACTIVITY IN THE LYMPHATIC TISSUES OF GERM-FREE NEW ZEALAND BLACK MICE. (E.) Denman, A. M. (Canadian Red Cross Mem. Hosp., Taplow, Berkshire, England) and E. J. Denman. *Int J Cancer* 6(1):108-122, 1970.

The incorporation of ³H-thymidine into the DNA of lymphoid cells in the thymus, spleen, lymph nodes and bone marrow of germ-free New Zealand Black mice of differing ages was measured quantitatively and by autoradiography to compare the proliferation of lymphoid cells at these sites in germ-free mice and conventional mice. Lymphoid cell proliferation,

particularly in splenic germinal centers, was the earliest abnormality noted in germ-free NZB mice and was equal in intensity to that observed in the conventional control strain. With the onset of autoimmune disease, reticulum cell and "blast" cell proliferation was qualitatively similar in the spleens of germ-free and conventional NZB mice, the former cell type predominating in the oldest mice examined. No evidence was obtained of any primary defect in lymphocytopoiesis in the thymus or other lymphatic tissues of the NZB strain. The onset of autoimmune disease in these mice may be preceded by lymphoproliferative changes; no differences were observed between germ-free and conventional animals or between males and females.

- 0169 INHERITANCE OF SUSCEPTIBILITY TO FRIEND MOUSE LEUKEMIA VIRUS: VII. ESTABLISHMENT OF A RESISTANT STRAIN. (E.) Odaka, T. (Inst. Med. Sci., Takanawa, Tokyo, Japan). *Int J Cancer* 6(1):18-23, 1970.

An attempt was made to place the gene for resistance to Friend leukemia virus in C57BL/6 mice, gene Fv^r, into the genetic background of susceptible mice of the DDD strain; the attempt was inspired by the finding that a single major autosomal locus controls susceptibility to Friend leukemia virus in mice. Using the cross-intercross system, the mice with Fv^r/Fv^r genotype were selected by progeny test at each even-numbered generation. During successive matings, the effect of gene Fv^r was not diluted out, and progeny were almost always obtained as expected from the single gene hypothesis. After 5 to 6 cycles of cross-intercross, brother-sister mating was done between the mice with Fv^r/Fv^r genotype. The progeny are homozygous for gene Fv^r and could be assumed to be congenic with DDD mice except for susceptibility to Friend leukemia virus. Locus Fv^r may be involved in cell proliferation rather than in virus multiplication, for, in mice of the new strain, the virus did not induce typical splenic megaly, but multiplied to a considerable level.

- 0170 ANTIGENIC MODIFICATION OF RAT TUMOR CELLS ARTIFICIALLY INFECTED WITH FRIEND VIRUS IN THE PRIMARY AUTOCHTHONOUS HOST. (E.) Sendo, F. (Hokkaido U. Sch. Med., Japan), H. Kaji, H. Saito and H. Kobayashi. *Gann* 61(3):223-226, 1970.

Tumors induced in rats by 3-methylcholanthrene were excised and artificially infected with Friend virus; these infected tumor cells when transplanted back into the autochthonous host did not grow well and later regressed spontaneously. However, transplanted non-infected primary tumor cells grew well and killed the autochthonous hosts, and infected primary tumor cells transplanted into Friend virus-tolerant rats grew well and killed the hosts. The virus infection appears to have modified the membranous antigens of the tumor cells to make them immunologically foreign to the autochthonous host.

- 0171 CHARACTERIZATION OF A RAPIDLY GROWING AKR LYMPHOBLASTIC CELL LINE MAINTAINING GROSS ANTIGENS AND VIRAL REPLICATION. (E.) Woods, W. A. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda,

Id.), N. A. Wivel, J. G. Massicot and M. A. Chirigos. *Cancer Res* 30(8):2147-2155, 1970.

Morphological and antigenic characteristics of a tissue culture system (AKR-A) established from an AKR ascitic cell line (from a spontaneous lymphoma found in a 9-month AKR mouse) are presented. The lymphoblastic cells (major cell type) are separated from the giant cells in primary cultures by utilizing the different growth rates, and the AKR-A cells can be maintained in the logarithmic phase of growth for 7 months. Antigen which was specific for GLV-infected cells, cellular antigen for anti-GLV serum, and the release of infectious GLV into the tissue culture fluid were observed in the AKR-A cells. *In vitro* passage of the AKR-A cells did not attenuate their tumor-producing capacity with the LD₅₀ in the male AKR mice remaining constant at 40 cells i.v.; the median survival time after 100 LD₅₀ was 11 days for AKR-A cells compared to 10 days for the AKR-ascites cells.

0172 GENETIC BASIS FOR SUSCEPTIBILITY TO LEUKEMIA INDUCTION BY AKR THYMUS GRAFTS. (E.) Takakuki, K. (Sch. Med., Mie Prefect. U., Japan). *Cancer* 61(1):85-87, 1970.

The influence of genetic constitution on the induction of leukemia by thymus grafts from high-leukemia strain AKR mice was investigated in F₁ hybrids of AKR and C3Hf or C57BL mice; (C3Hf x AKR)F₁ were homozygous for H-2^k and (C57BL x AKR)F₁ were heterozygous for H-2^k (H-2^{kb}). The incidence of leukemia was 17/22 in AKR mice, 23/34 in (C3Hf x AKR)F₁ mice and 0/22 in (C57BL x AKR)F₁ mice 104-180 days after AKR thymus grafting. None of the hybrid mice grafted with C3Hf or C57BL thymus of the same age developed leukemia. The leukemogenic capability of AKR thymus (Gross virus) and strain susceptibility appear to be influenced by genetic control.

0173 INFLUENCE OF PREDNISOLONE ON MOLONEY LEUKEMOGENIC VIRUS IN BALB/c MICE. (E.) Belson, H. T. (Child. Hosp. Med. Ctr., Boston, Mass.) and L. S. Rabstein. *Cancer Res* 30(8):2208-2212, 1970.

The effects of long term administration of prednisolone acetate (0.025 or 0.05 mg s.c. twice a week starting less than 24 hr after birth) on BALB/c mice response to Moloney leukemia virus were investigated. Lymphocytic leukemia developed in 0/83 mice given the high dose of prednisolone plus virus, in 60/78 mice given the low dose of prednisolone plus virus and in 83/92 mice inoculated with the virus alone. Significant numbers (at least 10%) of the infected prednisolone-treated mice developed solid lymphosarcomas or granulocytic leukemia compared to 1 occurrence of lymphosarcoma and no granulocytic leukemia in mice receiving virus alone; no tumors or leukemia were found in control animals. Inoculation of mice treated with the high dose prednisolone at 7 or 14 days after treatment was begun resulted in a 50% delay in onset of lymphocytic leukemia. The alteration in disease response may be attributed to a prednisolone-induced simulated thymectomy.

0174 HISTOPROLIFERATIVE EFFECT OF RAUSCHER LEUKEMIA VIRUS ON LYMPHATIC TISSUE. II. ANTIGEN-STIMULATED GERMFREE AND CONVENTIONAL BALB/c MICE. (E.) Hanna, M. G., Jr. (Oak Ridge Natl. Lab., Tenn.), H. E. Walburg, Jr., R. L. Tyndall and M. J. Snodgrass. *Proc Soc Exp Biol Med* 134(4):1132-1141, 1970.

Germfree mice received an i.p. injection of 1 ml of 1% sterile sheep erythrocytes followed by an infective i.p. injection of 0.5 ml Rauscher leukemia virus in order to establish a test system for studying the role of nonthymus-dependent and thymus-dependent lymphoid tissue in Rauscher leukemia virus infection; the leading hypothesis was that the splenomegaly associated with Rauscher disease in a germfree population would be enhanced by the establishment of active germinal centers in the nonthymus-dependent region of the lymphatic nodules of mice immunized with sheep erythrocytes. Ten days after viral infection, the sheep erythrocyte-pretreated mice exhibited 65% increase in spleen wt over the normal germfree mice. The retention by spleens of ¹²⁵I-iododeoxyuridine was also tested, with the result that sheep erythrocyte-immunized mice retained markedly more ¹²⁵I-iododeoxyuridine than unimmunized mice. Apparently, antigen-retaining reticular cells and immunoblasts of lymphatic tissue germinal centers play a necessary part in early lymphoblastosis and subsequent splenomegaly of Rauscher disease. Rauscher preparation seems, in addition, to have a differential effect on thymus and nonthymus-dependent regions of the lymphatic tissue, as indicated by morphologic results.

0175 TYPE-C PARTICLES IN HUMAN TISSUES: II. ELECTRON MICROSCOPIC STUDY OF EMBRYONIC CULTURES INFECTED WITH A MURINE LEUKEMIA VIRUS. (E.) Chandra, S. (John L. Smith Mem. Cancer Res., Charles Pfizer & Co., Maywood, N. J.), R. Stephens, B. S. Wright, W. Korol, I. Zelljadt and E. M. Jensen. *Int J Cancer* 6(1):46-55, 1970.

Human embryonic cultures were infected with the carcinogenic Rauscher murine leukemia virus to investigate the synthesis of type C virus particles by these cultures. Type C particles have the characteristic morphology of the murine leukemia viruses. In some cultures, type-C particles were also observed budding into the cisternae of rough endoplasmic reticulum of a few cells. Virus particles in the vicinity of such cells were of the immature type. In contrast, particles in the vicinity of those cells which did not synthesize intracisternal type-C particle were of the mature type. It is not clear whether or not the intracisternal particles and the mature extracellular type-C particles have the same morphology.

0176 DEOXYCHOLATE RELEASES RNA FROM RAUSCHER MURINE LEUKEMIA VIRUS. (E.) Smith, J. W. (St. Jude's Child. Res. Hosp., Memphis, Tenn.) and D. W. Kingsbury. *Proc Soc Exp Biol Med* 134(4):1039-1042, 1970.

A representative oncogenic RNA virus, Rauscher murine leukemia virus, was disrupted with deoxycholate and examined for subviral entities or nucleocapsids.

Deoxycholate treatment released RNA which sedimented at the same rate as the free RNA released by sodium dodecyl sulfate, a strongly ionic detergent. In virus which had been labeled in culture with ^{14}C -amino acids and then treated with deoxycholate, very little of the label was recovered with the viral RNA, indicating that little viral protein was associated with the released viral RNA. This RNA was completely sensitive to pancreatic ribonuclease, which indicates that the Rauscher murine leukemia virus probably does not reside in a subviral structure which resembles nucleocapsids isolated from nononcogenic enveloped RNA viruses.

- 0177 LOSS OF T ANTIGEN BY CELLS DERIVED FROM A HAMSTER TUMOR INDUCED BY ADENOVIRUS TYPE 12. (E.) Vasconcelos-Costa, J. (Gulberkian Inst. Sci., Oeiras, Portugal). *Int J Cancer* 6(1):24-30, 1970.

The effects of freezing on the morphology, growth, tumorigenicity, and tumor antigen synthesis of cells from an adenovirus type 12-induced hamster tumor were tested by freezing cells cultured from a second transplantation of such a tumor in liquid nitrogen and 10% dimethylsulfoxide. Subsequently these cells were cultured in the same conditions as the parent cells, where it was observed that they kept the morphological and growth characteristics and the tumorigenicity of the cells from the former culture. The synthesis of surface antigen was maintained but tumor antigen and tumor-specific transplantation antigen were not detectable. It cannot be conclusively stated that the freezing treatment or dimethylsulfoxide action was the cause of tumor antigen loss, although these are the most plausible explanations.

- 0178 INDUCTION OF INTERFERON IN CHICK CELLS BY ADENOVIRUSES OF DIFFERENT ORIGIN. (E.) Beladi, I. (U. Med. Sch. Szeged, Hungary), M. Bakay, R. Pusztai and G. Hidasi. *J Gen Virol* 8(2):143-144, 1970.

The induction of interferon in primary chick embryo fibroblast cells by canine hepatitis virus, bovine adenovirus, simian adenovirus and an avian virus was investigated, and compared to the interferon production by a human adenovirus. All adenoviruses studied induced interferon in chick cells, and the interferon-inducing ability of different adenoviruses was not dependent on the infective dose administered. Trypsin treatment did not reduce the infectivity of any of the adenoviruses. However, human and simian adenoviruses were not able to induce interferon after trypsin treatment, although trypsin-treated avian, bovine and canine types continued to induce interferon.

- 0179 ADENOVIRUS-ASSOCIATED VIRUSES: ENHANCEMENT BY HUMAN HERPESVIRUSES. (E.) Blacklow, N. R. (Natl. Inst. Allerg. Infect. Dis., Natl. Inst. Hlth., Bethesda, Md.), M. D. Hoggan and M. S. McClanahan. *Proc Soc Exp Biol Med* 134(4):952-954, 1970.

Studies were performed to examine any possible relationship between adenovirus-associated viruses

(AAV) and other human herpesviruses, Epstein-Barr virus, cytomegalovirus and varicella-zoster virus. Stock pools of AAV type 1(H) and AAV type 3(H) were heated for 15 min at 56°C to eliminate infectious adenovirus, and incubated with each of the other viruses in HEP-2 and WI38 cell cultures. All herpesviruses helped AAV1 to produce immunofluorescence antigen, but they were unable to elicit either the production of detectable AAV1 complement-fixing antigen or physical particles as viewed by electron microscopy. AAV1 immunofluorescence antigen was propagated only with adenovirus 7, but not with the other herpesviruses even at the second passage level, indicating that infectious AAV1 was produced only in the presence of adenovirus 7.

- 0180 DEMONSTRATION OF TWO GROUP-SPECIFIC TSTAS IN ADENOVIRUS-INDUCED TUMORS. (E.) Ankerst, J. (Dept. Med. Microbiol., U. Lund, Sweden) and H. O. Sjogren. *Int J Cancer* 6(1):84-94, 1970.

Mice and rats were infected with human adenovirus types of groups A, B, C and D (types 1, 3, 4, 5, 7, 12, 18 and 31) to determine whether infection would induce immunity to the tumor specific transplantation antigen. Colony inhibition tests were used to detect immunity. No immunity was induced by adenovirus of groups A and B (types 3, 7, 12, 18 and 31) against an adenovirus type 1 tumor; however, 2 adenovirus types belonging to group C (types 1 and 5) were similarly tested and found to induce a clear-cut immunity to the adenovirus type 1 tumor but not to tumors induced by adenovirus of groups A and B. The only tested virus type of group D (type 4) did not induce any clear-cut immunity to either adenovirus 12 tumors or the adenovirus 1 tumor. Immunization of rats with rat adenovirus 12 tumor cells induced a cellular immunity to adenovirus 12 mouse tumor cells but not to a mouse polyoma tumor; adenovirus 1 rat tumor cells induced no such immunity. Immunization of rats with syngenic adenovirus 12 tumor cells induced a cellular immunity to adenovirus 12 rat and mouse tumors and an adenovirus 7 hamster tumor, but not to an adenovirus 1 rat tumor or BHK-C13 control hamster cells. These results seem to be consistent with the existence of a common tumor specific transplantation antigen induced by types 7 and 12 and a different tumor specific transplantation antigen induced by type 5 virus. Apparently, the highly oncogenic group A and the weakly oncogenic group B adenovirus types all induce a common tumor specific transplantation antigen; and another tumor specific transplantation antigen is induced by the group C viruses, while no evidence has been obtained to indicate that group D virus types induce any tumor specific transplantation antigens.

- 0181 FATE OF ADENOVIRUS TYPES 2 AND 12 IN INFECTED SERIAL CULTURES OF NON-PRIMATE ORIGIN. (E.) Winters, D. (Natl. Inst. Med. Res., London, England) and N. Khoobyarian. *J Gen Virol* 8(2):95-104, 1970.

Rabbit heart fibroblast cells were inoculated with adenovirus, types 2 or 12, to investigate the development of infectious virus and antigens in the cultures. The formation of infectious virus and anti-

ns decreased with each successive passage of cells until the virus was ultimately eliminated from the cultures. These cultures then emerged into a new phase in which some virus-induced proteins were present in at least a small proportion of cells. Adenovirus 2 fiber antigen persisted throughout the 15th subculture, whereas adenovirus 12 early tumor and late fiber antigens were carried throughout the 30th subculture over a period of 600 days. Virus-free but antigen-containing cells may therefore have possessed at least a portion of the virus genome. Shortly after the disappearance of virus, distinct multilayered foci of cells emerged in both lines; but only in the adenovirus 12 line did this phenomenon appear as a characteristic feature of the culture.

82 TUMOR INDUCTION IN HAMSTERS WITH AN AVIAN ADENOVIRUS (CELO): BRIEF REPORT. (E.) Mancini, L. O. (Union Carbide Res. Inst., Tarrytown, N. Y.), J. Anderson, V. Jasty and V. J. Jasty. *Arch Ges Virusforsch* 30(2-3):261-262, 1970.

Partially purified chicken-embryo-lethal-orphan virus, either untreated, irradiated, or mixed with 10% chicken embryo extract, tumor extract or 10% sucrose was injected into hamsters intradermally, intracranially or subcutaneously to determine if the treatment or the method of inoculation could affect the time and percentage of tumor induction. Hamsters inoculated intracranially with the virus alone or with chicken embryo extract produced epimomas in 33% and 22% of the animals, resp., in 14 weeks; subcutaneous inoculation with virus and embryo extract resulted in fibrosarcoma formation in 42% of the animals in 9 weeks. The other procedures and mixtures produced no tumors or induced tumors at a low rate and over a longer time interval.

83 THE SPECIFICITY OF ADENOVIRUS-HUMAN SERUM INHIBITOR INTERACTION. (E.) Shortridge, F. (U. Coll. Hosp. Med. Sch., London, England). *Arch Ges Virusforsch* 30(2-3):238-244, 1970.

Electrostatically separated surface components of hemagglutinating adenovirus type 5 and the soluble antigens of this virus were reacted with a known hemagglutinating virus inhibitor to study the specificity of the ensuing interaction. The nonspecific inhibitor of adenovirus hemagglutination combined with hexons (soluble and viral) as well as with the hemagglutinating entities to produce flocculation. Therefore the hemagglutination inhibition test was best performed using either penton or fiber antigen as indicator; the fiber was preferable because of its stability. The inhibitor appeared to combine specifically with the hexons proper; the adjacent hexons and/or peripentons may be responsible for attachment of virus to the host cell. These results underline the importance of the use of serum inhibitors in the elucidation of the nature of the viral surface and the relationship of that surface to red blood cell and host cell systems. Chemical identification of the active groupings involved may elucidate the fundamentals of the infective process.

0184 THE RESPONSE OF BHK 21 CELLS TO INFECTION WITH TYPE 12 ADENOVIRUS: III. TRANSFORMATION AND RESTRICTED REPLICATION OF SUPERINFECTING TYPE 2 ADENOVIRUS. (E.) Strohl, W. A. (Rutgers Med. Sch., New Brunswick, N. J.), H. Rouse, K. Teets and R. W. Schlesinger. *Arch Ges Virusforsch* 31(1-2):93-112, 1970.

A clonal line of hamster cells (BHK 21) was subjected to high multiplicity infection with adenovirus (type 12) to investigate the transformation response of the cells; a transformation rate of approximately 2×10^{-5} per initially infected cell was observed. A study of the fate of the abortively infected cells revealed, however, that only a small fraction survived the infection and initiated growth of a colony. Of these rare surviving colonies, nearly half contained transformed cells. Of 3 cell sublines tested, 1 yielded transformed cells only from colonies growing in soft agar suspension, a second yielded transformants only as foci in monolayers, while the third did not yield detectable transformants by either method. The adenovirus-transformed cells were distinguished from the parental cells by the following characteristics: a marked morphological alteration; the synthesis of adenovirus tumor antigen; growth to high cell density in the presence of a low concentration of serum; induction, in hamsters, of tumors identical to those induced by inoculation of type 12 virus; and restriction in the ability to support the multiplication of type 2 adenovirus (Ad2). The latter property may be due to blockage of a step late in the adenovirus replicative cycle, since 88% of the cells, which synthesized adenovirus type 2-specific structural antigens did not yield infectious virus. A similar shift from a productive to a largely abortive response to adenovirus 2 was seen in cells simultaneously infected with adenovirus 12 and adenovirus 2. Apparently, an association exists between continued activity of part of the adenovirus type 12 genome and the restriction of adenovirus type 2 replication in adenovirus type 12-transformed cells.

0185 SARCOMAS AFTER INOCULATION OF NEWBORN HAMSTERS WITH *HERPES VIRUS HOMINIS* TYPE 2 STRAINS. (E.) Nahmias, A. J. (Emory U. Sch. Med., Atlanta, Ga.), Z. M. Naib, W. E. Josey, F. A. Murphy and C. F. Luce. *Proc Soc Exp Biol Med* 134(4):1065-1069, 1970.

Doses greater than 10^3 TCD₅₀ of *Herpes virus hominis*, type 1 or 2, injected into newborn hamsters caused nearly 100% mortality, while lesser doses produced sarcomas 5-28 months after inoculation of 5 different virus strains. None of the animals inoculated with *Herpes virus hominis* type 1 strains developed tumors, and one newborn hamster inoculated intrathoracically with Eagle's MEM developed a well-differentiated cheek-pouch fibrosarcoma. Eight of 9 tumors with *Herpes virus hominis* type 2 strains occurred at or close to the site of inoculation and the histological characteristics of some of these tumors differed from those associated with other viral-induced hamster sarcomas. There is no clear-cut evidence of a relationship between *Herpes virus hominis* and the tumors, although C-type particles were observed by electron microscopy in 2 or 3 tumors.

- 0186 ANTIBODY TO GENITAL HERPES SIMPLEX VIRUS: ASSOCIATION WITH CERVICAL ATYPIA AND CARCINOMA *IN SITU*. (E.) Aurelian, L. (Johns Hopkins Sch. Med., Baltimore, Md.), I. Royston and H. J. Davis. *J Nat Cancer Inst* 45(3):455-464, 1970.

The prevalence of antibodies to the genital variant of herpes simplex virus (HSV-2) in sera of 36 women with atypia and of 32 women with carcinoma *in situ* (30-35 yr average age) and in women with invasive carcinoma (53 yr average age) was compared to a matched control population. The occurrence of antibody to HSV-2 was 100% in patients with invasive carcinoma and carcinoma *in situ* and 95% in women with cervical atypia, but only 50% in the control population. The data support the hypothesis that genital herpes simplex virus may be responsible for squamous neoplasia in the human cervix. Detection of viral components in neoplastic cells is needed for further substantiation of the possible relationship of HSV-2 and cervical carcinoma.

- 0187 HERPESVIRUS TYPE 2 INFECTION AND CARCINOMA OF THE CERVIX. (E.) Sprecher-Goldberger, S. (Brabant Pasteur Inst., Brussels, Belgium), L. Thiry, J. P. Cattoor, R. Hooghe and J. Pestiau. *Lancet* 2(7666):266, 1970.

The association of genital herpes simplex virus type-2 infection with cervical carcinoma in Belgium was demonstrated by vaginal exfoliative cytology and by the observation of specific neutralizing antibodies to herpesvirus type-2 in patients with cervical carcinoma. Serum samples were obtained from patients with invasive carcinoma of the cervix and compared with samples from patients without cervical carcinoma. The results confirm that women with invasive carcinoma of the cervix have a high incidence (83%) of antibodies to herpes virus type-2. Herpetic infection was quite evidently localized among cervical cancer patients, for all patients studied had been exposed to the same risk of herpes infection.

- 0188 INHIBITION OF HERPES VIRUS-INDUCED GIANT CELL FORMATION BY COMPOUND 48/80. (Ger.) Falke, D. (Inst. Med. Microbiol., Johannes Gutenberg U., Mainz, Germany) and G. F. Kahl. *Arch Ges Virusforsch* 30(4):353-366, 1970.

Herpes virus-induced giant cell formation in a rabbit kidney cell culture was inhibited by the histamine releasing compound 48/80. Vacuolization of the cell cytoplasm occurred 6 hr after compound 48/80 administration; these vacuoli appeared to be a result of lysosomal activation which was confirmed by acid phosphatase determinations. Comparison of structural analogs of the monomer of compound 48/80 and Resochin in terms of inhibition effects of giant cell formation, lysosomal activation and histamine release revealed that Resochin activated the lysosomes at 1 µg/ml and blocked giant cell formation at a concentration of 50 µg/ml, producing no histamine releasing effects. Compound 48/80 released histamine at a concentration of 0.1 µg/ml, blocked giant cell formation at 10 µg/ml concentration and activated

lysosomes at 50 µg/ml concentrations. Lysosomal enzymes did not enhance herpes virus-induced giant cell formation.

- 0189 VIRUSES AND RENAL CARCINOMA OF *RANA PIPIENS*: IX. THE INFLUENCE OF TEMPERATURE AND HOST CELL ON REPLICATION OF FROG POLYHEDRAL CYTOPLASMIC DEOXYRIBOVIRUS (PCDV). (E.) Gravell, M. (St. Jude Child. Res. Hosp., Memphis, Tenn.) and A. Granoff. *Virology* 41(4):596-602, 1970.

Cells from fathead minnow, baby hamster kidney and chicken embryo were incubated in temperature ranges from 8-33°C to study the replication of a polyhedral cytoplasmic deoxyribovirus obtained from tumor-bearing frogs. No significant virus replication occurred in any cell type at either 8°C or 10°C, but at 12°C replication occurred in all cell types used. However, yields of polyhedral cytoplasmic deoxyribovirus and rate of production at 12°C were greater in cells from cold-blooded than from warm-blooded vertebrates. Furthermore, the viral latent period at 12°C was shorter in fathead minnow cells (12-24 hr) than in either baby hamster kidney (2-3 days) or chicken embryo cells (3-4 days). As the temperature was raised from 12 to 30 or 31°C, the viral latent period decreased, the rate of multiplication increased, and high titers of infectious virus were obtained over a broad temperature range in all cells. At 30°C to 31°C, there was little difference in the latent periods or in the rates of polyhedral cytoplasmic deoxyribovirus replication in cells originating from poikilotherms or homeotherms. Irrespective of cell type, both yield and rate of virus replication were reduced at 32°C. Infectious progeny virus was not made in any cell type at 33°C, but virus-specific macromolecules were formed at this temperature. Data from temperature shift experiments (33.5°C → 24°C) suggested that a temperature-sensitive event occurred late in the virus replication cycle, possibly at assembly of viral components. The virus yield and replication rate appear to be controlled by the host cell, although the permissive temperature for replication is controlled by the viral genes.

- 0190 STUDIES ON THE MAMMARY TUMOR AGENT (MTA): I. COMPARATIVE CYTOCHEMISTRY OF NUCLEIC ACID AND PROTEINS IN NORMAL RIIIf, C57BL MAMMARY GLANDS, AND IN MALIGNANT CELLS OF SPONTANEOUS MAMMARY TUMORS OF RIII AND VIRUS-INDUCED TUMORS IN C57BL. (E) El-Fiky, S. M. (Inst. Med. Res., Camden, N. J.). *Acta Histochem* 36(2):356-367, 1970.

Metabolic alterations in tumor cells of mice bearing both spontaneous (RIII strain) and virus-induced (C57BL and RIIIf) mammary adenocarcinoma were investigated by cytochemical estimations of RNA, DNA, and total and basic proteins in tumor cells. No significant differences in the topographical distribution of RNA, DNA, total and basic proteins were observed. However, the concentration of all of these constituents decreased from highest in tumor cells of spontaneous mammary tumors, followed by virus-induced tumor cells, and then normal mammary gland epithelium. No difference in the intensity of the cytochemical parameters studied was detected for cells of normal mammary glands of the 2 strains. The difference

in concentrations of nucleic acids and basic proteins in virus-induced C57BL tumors compared to spontaneous tumors in RIII mice could be due to alterations of the microchemical environment favoring the synthesis and release of virus and leading to the suppression of the metabolic rate of induced tumor cells.

- 0191 UNIQUE GLYCOPROTEIN FROM MOUSE MILK CONTAINING THE MAMMARY TUMOR AGENT. (E.) Miroff, G. (Dept. Biol., Union Coll., Schenectady N. Y.), H.M. Meade, M. Winetroun and H.V. Lamberson. *Nature* 227(5264):1243-1244, 1970.

A unique chemical determinant which is antigenic in rabbits was isolated and identified in mouse milk containing the mammary tumor agent. The isolation and purification process included CaCl_2 precipitation, ammonium sulfate precipitation, ECTEOLA-cellulose chromatography, Sephadex G-100 column chromatography, and preparative disc electrophoresis. The isolated antigen was not inactivated by neuraminidase, amylase, lysozyme, or chloroform-methanol extraction, but was inactivated when heated for 1 hr at 70°C or treated with pronase at 37°C for 1 hr.

- 0192 MOUSE STRAIN AND BREEDING STIMULATION AS FACTORS INFLUENCING THE EFFECT OF THYMECTOMY ON MAMMARY TUMORIGENESIS. (E.) Squartini, F. (Med. Sch. Pisa, Italy), M. Olivi and G. B. Bolis. *Cancer Res* 30(7):2069-2072, 1970.

Thymectomies were performed on newborn BALB/cf(C3H), BALB/cf(RIII), and RIII strain mice which carried spontaneous mammary tumor virus infection to determine the effect of this operation on tumorigenesis. In BALB/cf(C3H) virgin females, thymectomy decreased mammary tumor incidence from 82 to 46% and delayed tumor onset by about 5 months; in BALB/cf(RIII) force-fed females, thymectomy delayed tumor onset by about 2 months but did not significantly affect the final mammary tumor incidence. In RIII females, either virgins or breeders (normal and force-bred), thymectomy had no effect on frequency and onset of mammary tumors. Mouse strain and breeding condition does appear to influence the effect of thymectomy and the immunological responsiveness of the host animal to virus induced tumorigenesis.

- 0193 MAMMARY TUMORS IN STRAINS BL/LyDe AND SWR/LyDe MICE. (E.) Deringer, M. K. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *J Nat Cancer Inst* 45(2):215-218, 1970.

The presence of mammary tumor virus was demonstrated in strain BL/LyDe mice by the induction of mammary tumors in agent-free substrains C3Hf/HeDe and C3HeB/De mice foster-nursed by BL/LyDe mice. The incidence of mammary tumors in breeding females of strain BL/LyDe was 10% at an average age of death of 15.5 months, while the incidence of mammary tumors in foster-nursed females of strains C3Hf/HeDe and C3HeB/De at an average age of 18 months was 47% (controls, 2% and 4%). The types of mammary tumors produced were adenocarcinomas Type A and Type B. The incidence of mammary tumors in C3Hf/HeDe and C3HeB/De

foster-nursed by SWR/LyDe females was 4% at an average age of death of 25 months, indicating that strain SWR/LyDe mice either do not possess mammary tumor virus or do not transmit it to foster-nursed animals.

- 0194 MOUSE MAMMARY TUMOR VIRUS INFECTIVITY AS A FUNCTION OF AGE AT INOCULATION, BREEDING, AND TOTAL LAPSED TIME. (E.) Moore, D. H. (Inst. Med. Res., Camden, N. J.), J. Charney and B. D. Pullinger. *J Nat Cancer Inst* 45(3):561-565, 1970.

Mouse mammary tumor virus-containing milk (tumor incidence, 84%) was injected i.p. into tumor- and virus-free mice at from 2-12 wk after birth at doses of 0.2 ml/mouse to investigate the effect of inoculation age on viral infection and its correlation with the eventual development of mammary tumors; antigen was assayed with rabbit anti-mammary tumor virus antiserum on micro-Ouchterlony plates. Over the age range of 2-10 wk, the total lapsed time from inoculation to the appearance of antigen in the milk or the development of tumors was approximately constant, irrespective of age at inoculation; however, inoculation at 12 wk of age gave a relatively lower incidence of infection and tumor development. All age groups had a gradual increase in antigen incidence from the first to the third lactation. Force-breeding to the second or third lactation of mice inoculated at age 10 and 12 wk did not shorten the lapsed time for obtaining equivalent antigen incidences. Inoculation during first pregnancy gave negative antigen-assay results at the third and even at the sixth lactation. Inoculating mice at ages between 4 and 10 wk, mating them at 10-12 wk, and testing their milk at the second lactation gave a practical assay requiring about 15 wk.

- 0195 ISOLATION OF MURINE SARCOMA VIRUS-TRANSFORMED MOUSE CELLS WHICH ARE NEGATIVE FOR LEUKEMIA VIRUS FROM AGAR SUSPENSION CULTURES. (E.) Bassin, R. H. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), N. Tuttle and P. J. Fischinger. *Int J Cancer* 6(1):95-107, 1970.

A subline of mouse 3T3 cells was infected with the Moloney isolate of murine sarcoma virus, and colonies of transformed cells were produced in semi-solid agar suspension cultures. At optimal cell concentrations, the number of colonies formed was proportional to the concentration of murine sarcoma virus, although the same virus preparation gave 2-hit titration patterns in focus assays using monolayer cultures of 3T3 cells. Individual colonies were picked from agar suspension cultures and grown as monolayers. Some of the colonies selected gave rise to cell lines which yielded detectable quantities of focus-forming murine sarcoma virus, while others did not. Five lines which did not yield detectable murine sarcoma virus were superinfected with murine leukemia virus; focus-forming murine sarcoma virus was subsequently detected in 3 of the 5 lines. These 3 lines, therefore, probably contain the murine sarcoma virus genome in the absence of infectious leukemia virus and are termed "sarcoma-positive leukemia-negative" mouse cells.

One sarcoma-positive leukemia-negative cell line, in addition to releasing murine sarcoma virus after superinfection with murine leukemia virus, responded with the formation of murine sarcoma virus-type foci in proportion to the concentration of murine leukemia virus used for superinfection. This line is composed of two morphological cell types, one indistinguishable from murine sarcoma virus-transformed 3T3 cells and the other normal in appearance. Focus formation in this cell line has been used to develop an assay system for Friend, Moloney and Rauscher leukemia viruses. Colony formation in semi-solid agar appears to be an effective means of separating murine sarcoma virus infection and cell transformation from murine leukemia virus infection and replication.

- 0196 USE OF A MURINE SARCOMA VIRUS IN AN *IN VIVO* ASSAY FOR ANTIVIRAL AND ANTITUMOR AGENTS. (E.) Pearson, J. W. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), W. T. Gibson and M. A. Chirigos. *Cancer Res* 30(7):2024-2028, 1970.

A plasma variant of the Moloney sarcoma virus with infection characteristics suitable for evaluation of potential antiviral agents is described. Inoculation i.p. of this virus into adult mice resulted in a progressive splenomegaly. The enlarged spleens were firm and contained multiple cream-white areas, and inguinal and cervical lymph nodes were enlarged markedly. The degree of splenomegaly was dependent on the initiating dose of virus, which permits the use of spleen weight as a parameter for quantitative measurement of virus titer. Extracellular virus was recoverable from the plasma 3 days after infection, before there was any significant increase in spleen weight; in addition, virus was recoverable from infected spleen and liver 5 days after inoculation. Two drugs, melphalan and 1,3-bis(2-chlorethyl)-1-nitrosourea tested for antiviral activity against the murine sarcoma virus (plasma variant Moloney strain), were effective in retarding splenomegaly, decreasing virus titer, and increasing median survival time.

- 0197 ACCELERATION BY THYMOSIN OF THE DEVELOPMENT OF RESISTANCE TO MURINE SARCOMA VIRUS-INDUCED TUMOR IN MICE. (E.) Zisblatt, M. (Albert Einstein Coll. Med., Yeshiva U., Bronx, N. Y.), A. L. Goldstein, F. Lilly and A. White. *Proc Nat Acad Sci* 66(4):1170-1174, 1970.

Moloney murine sarcoma virus was inoculated into mice of various ages that were injected with a liver or spleen extract or with thymosin from day 2-14 after birth to study the effect of the thymic extract on the development of resistance to progressive tumor growth. Resistance in CBA/Wh mice, at the virus dose used, was first detected at approximately 2 wk of age and was completely developed at 5 wk. Thymosin administration to newborn mice significantly accelerated the rate of development of resistance to progressive tumor growth; thymosin-treated mice challenged with virus at 2 wk had the same survival rate as control animals of 3 wk. Liver- and spleen-treated mice did not differ from control. The data suggest a humoral role for the thymus in the development of tumor immunity and that the use of thymus-

derived extracts can accelerate the development of cell-mediated immunological competence.

- 0198 RADIOLOGICAL STUDIES ON THE CHRONOLOGICAL RELATION BETWEEN MURINE SARCOMA VIRUS INFECTION AND CELL CYCLE. (E.) Yoshikura, H. (Fac. Sci. Orsay, France). *J Gen Virol* 8(2):113-120, 1970.

Cell cultures originating from kidney tissues of newborn mice were infected with murine sarcoma virus and subjected to UV irradiation (10 ergs/mm²/sec) to investigate the intracellular replication of the virus as affected by UV. In experiments with unsynchronized cultures UV sensitivity of the cells infected with murine sarcoma virus as focus centers increased with the lapse of time after infection, and 16 hr after infection UV-resistant cells appeared which were probably producing mature virus. The UV-resistant population continued to increase thereafter. Ultraviolet sensitivities as focus centers of synchronized cells infected with murine sarcoma virus at different periods of the cell cycle were compared 23 hr after infection. The cells infected with the virus in the G1 phase remained more sensitive to UV light than those infected with the virus in the S phase, resulting in a longer latent period after G1 phase infection than after S phase infection. An antimitotic agent, colchicine, prevented the increase of UV resistance of the cells as focus centers. The findings indicate that virus replication is synchronized at the stage of host cell division in the cell cycle, and that murine sarcoma virus infection requires division of host cells.

- 0199 MURINE SARCOMA VIRUS TRANSFORMATION OF BALB/3T3 CELLS: LACK OF DEPENDENCE ON MURINE LEUKEMIA VIRUS. (E.) Aaronson, S. A. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), J. L. Jainchill and G. J. Todaro. *Proc Nat Acad Sci* 66(4):1236-1243, 1970.

The pattern of focus formation induced by murine sarcoma virus in mouse cells was studied in BALB/3T3 cells. Early after infection with murine sarcoma virus (and murine leukemia virus which is present in murine sarcoma virus stocks), the pattern of focus formation was "two-hit" or one which required the presence of both viruses in the initially infected cell. However, after 7 days, the focus formation pattern became "one-hit" or one which was entirely dependent upon cell division of the originally infected cell and which was due to infection by murine sarcoma virus alone. The "two-hit" pattern resulted from the inability to detect the "one-hit" foci early after infection. These data indicate that murine sarcoma virus is able to transform mouse cells without requiring murine leukemia virus.

- 0200 TUMORS INDUCED IN THE SOUTH AMERICAN MARMOSET MONKEY BY ROUS SARCOMA VIRUS. (E.) Noyes, W. F. (Sloan-Kettering Inst. Cancer Res., New York, N.Y.). *J Nat Cancer Inst* 45(3):579-587, 1970.

The Carr-Zilber and Schmidt-Ruppin strains of the Rous sarcoma virus were used to induce metastasizing

epoasms in newborn and adult South American marmosets. Two of 8 adult cottontop marmosets [*Saguinus oedipomidas*] inoculated with the Carr-ilber strain developed slowly growing fibrosarcomas and spindle cell sarcomas; while 11 of 12 adult cottontop marmosets and white-lipped tamarin marmosets (*S. nigricollis* group) inoculated with the Schmidt-Ruppin strain developed rapidly growing round cell and spindle cell sarcomas, frequently with multinucleated giant cells. These tumors frequently became very large (25-45 cm²) and metastasized regularly to lymph nodes but infrequently to the lungs. Death from Schmidt-Ruppin-induced tumor in adults usually occurred in 6-8 weeks. In newborn animals inoculated with this strain, the latent period was as short as 25 days before the development of invasive and metastatic spindle and round cell sarcomas, and terminal stages were reached in 3-6 weeks. Two adult marmosets developed sarcomas after inoculation with a cell-free filtrate of the Schmidt-Ruppin strain. No spontaneous neoplasms were observed in the marmoset colony over a 6-year period.

0201 A FULL EXPRESSION OF THE GENOME OF ROUS SARCOMA VIRUS IN HETEROKARYONS FORMED AFTER FUSION OF VIROGENIC MAMMALIAN CELLS AND CHICKEN FIBROBLASTS. (E.) Machala, O. (Czechoslovak Acad. Sci., Prague), L. Donner and J. Svoboda. *J Gen Virol* 8(3): 19-229, 1970.

Inactivated Sendai virus was used to obtain cell fusion of virogenic hamster cells and indicator chicken cells; immunofluorescence and autoradiographic tests were performed which indicated that all heterokaryotic cells formed after fusion produced Rous sarcoma virus coat antigen. Homokaryons and mononuclear cells of both types were negative in the immunofluorescence test. Similarly, all tested single heterokaryons obtained by visually controlled cell fusion produced infectious Rous sarcoma virus. Virus coat antigen or infectious virus was not formed in virogenic cells or chicken fibroblasts agglutinated but not fused in the mixture with Sendai virus, or in heterokaryons obtained after fusion of virogenic cells with chicken erythrocytes, including heterokaryons containing 'reactivated' chicken erythrocyte nuclei. An important role in the process for Rous sarcoma virus appears to be played by heterokaryons formed after fusion of virogenic cells with chicken fibroblasts, which seem to be permissive cells for that virus.

0202 GLYCOPROTEIN COMPONENTS OF AVIAN AND MURINE RNA TUMOR VIRUSES. (E.) Duesberg, P. H. Virus Lab., U. California, Berkeley), G. S. Martin and P. K. Vogt. *Virology* 41(4):631-646, 1970.

Component isolation procedures carried out on different strains of Rous sarcoma virus and Rauscher mouse leukemia virus resulted in the isolation of glycoproteins containing glucosamine, galactose and fucose. Polyacrylamide gel electrophoresis in sodium dodecyl sulfate indicated that the molecular weight of the major glycoprotein of Rous sarcoma virus was between 90,000-105,000 daltons, depending on the strain of the virus; the minor glycoprotein had an

approximate molecular wt of 37,000. Both glycoproteins had higher molecular wts than the proteins of the group specific antigen of avian tumor viruses. The glycoproteins represented between 10% and 20% of the radioactive protein of purified virus. Disruption of Rous sarcoma virus with sodium dodecyl sulfate yielded glycoprotein components with sedimentation coefficients between 4 S and 2 S. The glycoprotein derived from Tween 20-disrupted virus was obtained in a 4-2 S form and in an 8 S form. The 8 S component consisted predominantly of a multimeric aggregate of the two viral glycoprotein components, and some group-specific antigen. Glycoproteins of different strains of avian tumor virus are probably part of or identical with the viral type- or subgroup-specific antigen, since both the 8 S and the 4-2 S glycoprotein derived from Tween 20-disrupted Rous sarcoma virus specifically inhibited virus neutralizing antibody, and since the glycoproteins of different strains of Rous sarcoma virus had different electrophoretic mobilities.

0203 PRESENCE OF DNA IN ROUS SARCOMA VIRUS. (E.) Levinson, W. (Dept. Microbiol. U. California, San Francisco), J. M. Bishop, N. Quintrell and J. Jackson. *Nature* 227(5262):1023-1025, 1970.

DNA was isolated from purified Rous sarcoma virus (Schmidt-Ruppin strain). The virus was doubly labeled with ³H-thymidine and ¹⁴C-uridine and analyzed by isopycnic centrifugation. The labeled nucleic acid extracted from the virus was sensitive to deoxyribonuclease, but not to ribonuclease or 1 M NaOH. When sonicated ³H-thymidine-labeled uninfected chick embryo cells and unlabeled Rous sarcoma virus were mixed and purified by centrifugation, no ³H-thymidine counts were associated with the purified virus, establishing that the DNA isolated from the virus was an intraviral entity and not cellular DNA. The bulk of the DNA sedimented slightly ahead of the 4S RNA of the virus and a small part cosedimented with the 65S RNA; electrophoretic migration patterns indicated that the 65S DNA was not covalently linked to 65S RNA.

0204 ANALYSIS OF A FUNCTIONAL CHANGE IN MEMBRANE IN THE PROCESS OF CELL TRANSFORMATION BY ROUS SARCOMA VIRUS: ALTERATION IN THE CHARACTERISTICS OF SUGAR TRANSPORT. (E.) Hatanaka, M. (Publ. Hlth. Res. Inst. New York, New York) and H. Hanafusa. *Virology* 41(4):647-652, 1970.

Alterations in the kinetics of the uptakes of glucose and some other sugars coincident with the morphological changes occurring during the process of Rous sarcoma virus infection were studied in chick embryo cells. An increase in the uptake of D-glucose, 2-deoxy-D-glucose and D-glucosamine (assayed by isotope uptake) was first observed at 16 hr after inoculation of the culture; at this time morphological changes also became recognizable in 15% of the cell population. The ratio of uptake into infected to that into noninfected cultures at 42 hr postinfection were 13.3, 8.4 and 21.9 for D-glucose, 2-deoxy-D-glucose and D-glucosamine, resp. In infected cultures with glucose in the medium, the decrease in glucose was accompanied by a concomitant

increase in lactic acid. The uptake of 2-deoxy-D-glucose seemed to follow most closely the degree of cell transformation in infected cultures. A non-transforming C type particle (RAV-2) infection of chick embryo cells showed no alterations in sugar transport.

- 0205 ROUS SARCOMA VIRUS: A FUNCTION REQUIRED FOR THE MAINTENANCE OF THE TRANSFORMED STATE. (E.) Martin, G. S. (Virus Lab., U. California, Berkeley). *Nature* 227(5262):1021-1023, 1970.

The isolation of a temperature-sensitive mutant of the Schmidt-Ruppin strain of Rous sarcoma virus, the properties of which indicate that mutation affects a function required for the maintenance of the transformed state but not for growth of the virus, is described. Survivors of a crude stock of SR-RSV-A virus which had undergone mutagenic treatment with N-methyl-N'-nitro-N-nitrosoguanidine (2 mg/ml) were cloned at 35-36°C using an agar suspension of chick fibroblasts. One of the 6 mutants isolated which were able to form foci at 36°C but not at 41°C was selected for study. The rate of virus accumulation and the rate of inactivation was the same for both the mutant and the wild type at 41°C, indicating that mutation did not affect the growth of the virus. When T1-transformed cells (at 36°C) were shifted to 41°C, the cells rapidly lost their rounded refractile appearance and assumed a near-normal appearance within 4 hr; cells infected by the wild type virus were unaffected by the temperature shift. The reverse change, when T1-infected cells grown at 41°C were shifted to 36°C and became completely transformed, was slower, taking about 2 days. Part of the viral genome required for maintenance of the transformed state is apparently lost or inactivated at the non-permissive temperature in this mutant, although its growth is not affected.

- 0206 CHARACTERISTICS OF CORES OF AVIAN LEUKO-SARCOMA VIRUSES. (E.) Bader, J. P. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), N. R. Brown and A. V. Bader. *Virology* 41(4):718-728, 1970.

Mixtures of the tumorigenic Rous sarcoma virus and Rous associated virus were treated with Tween 80 in ethyl ether, phospholipase A or C, and density gradient centrifugation. Cores labeled with ³H-uridine had a density (1.27 g/ml) different from intact virus (1.16 g/ml) and could be separated by isopycnic banding in potassium tartrate, cesium sulfate, or sucrose gradients. The viral RNA within the cores was susceptible to ribonuclease, and the general instability of cores may be partly explained on this basis. Cores obtained from murine leukemia virus had properties similar to those of Rous sarcoma virus and Rous associated virus. Density-purified cores exhibited complement-fixing activity when mixed with group-specific antiserum, but most of the group specific antigen was solubilized during processing of virions. The findings suggest that the virion core probably plays a role only in the absorption and penetration of cells, and that intact cores are infectious only if access to the cell is provided.

- 0207 SENDAI VIRUS RNA AS MESSENGER RNA DETERMINING THE SYNTHESIS OF EARLY VIRUS SPECIFIC PROTEINS. (E.) Mekler, L. B. (Acad. Med. Sci., Moscow, USSR), M. A. Shlyankevich and V. J. Shevliaghyn. *Arch Ges Virusforsch* 30(4):309-315, 1970.

The effect of Sendai virus inactivated by ultraviolet irradiation (BUV-30 germicidal tube at 6 cm for 12 min) or β -propiolactone (final concentration of 0.1%) on cell properties was studied in an HRT-CEF cell mixture (hamster Rous tumor and chick embryo fibroblast cells). The inactivated virus induced synthesis of early virus-specific proteins (virus-induced cell antigen) without virus-specific RNA, suggesting that mRNA for the synthesis of early proteins of Sendai virus is the virion RNA (plus strand). Only one strand of viral nucleic acid is transcribed in the cell and if the structural proteins are coded in the minus strand, the absence of structural protein synthesis with the inactivated virus is obvious.

- 0208 CELO VIRUS: AN ONCOGENIC VIRUS: BRIEF REPORT. (E.) Mancini, L. O. (Union Carbide Res. Inst., Tarrytown Tech. Ctr., N. Y.), V. J. Yates, J. Anderson and V. Jasty. *Arch Ges Virusforsch* 30(2-3):257-260, 1970.

The chicken-embryo-lethal-orphan (CELO) virus was established as an oncogenic virus in golden Syrian hamsters in this study. Infectious virus particles were isolated from the cell suspensions of 2 tumors, from the pelleted extracts of 3 neoplasms, and from tumor cell cultures; various control systems failed to yield infectious virus particles. Plaque purified CELO virus was mixed with an equal amount of undiluted serum from tumor-bearing or normal hamsters and was allowed to incubate at room temperature for 1 hr; embryonated eggs were inoculated with the various samples via the allantoic sac. Protection, as indicated by viable healthy embryos after 10 days, was proof of the presence of type-specific CELO antibody in the tumored hamsters; sera from control animals failed to neutralize the test dose. When hamsters immunized with CELO virus were challenged with tumor cells the transplants were completely rejected; polyoma and Schmidt-Ruppin Rous sarcoma tumor cells produced tumors in both the CELO-immunized and non-immunized hamsters at the same rate. These data, along with the finding of type specific CELO "T" antigen in tumor cells by the fluorescent antibody technique, confirm the oncogenicity of CELO virus.

- 0209 VIRUS-SPECIFIED DEOXYRIBONUCLEIC ACID IN SIMIAN VIRUS 40-EXPOSED HAMSTER CELLS: CORRELATION WITH S AND T ANTIGENS. (E.) Levine, A. S. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), M. N. Oxman, P.H. Henry, M. J. Levin, G. T. Diamandopoulos and J. F. Enders. *J Virol* 6(2):199-207, 1970.

Hamster embryonic cell lines infected by SV40 were examined for the presence of cellular DNA complementary to tritiated viral RNA synthesized *in vitro* by hybridization techniques. The methods employed permitted the detection of 10^{-5} μ g of viral DNA in 100 μ g of cellular

NA, corresponding to one-fifth of an SV40 DNA molecule per cell. Those lines which contained both the SV40 surface (S) and tumor (T) antigens also contained DNA complementary to SV40 RNA synthesized *in vitro*. In contrast, neither of two lines which contained surface, but not tumor antigen contained detectable DNA complementary to SV40 RNA. Although current methodology cannot exclude the presence of a single copy of one viral gene per cell, these results suggest that the continued synthesis of S antigen does not require the persistence of SV40 DNA in the transformed cells.

0210 THYMIDINE KINASE ACTIVITY AND DNA SYNTHESIS IN CELLS INFECTED WITH THE PARVOVIRUS H-1. (E.) Fong, C. K. Y. (Putnam Mem. Hosp. Inst. Med. Res., Bennington, Vermont), N. Ledinko and H. W. Toolan. *Proc Soc Exp Biol Med* 134(4):1199-1203, 1970.

Simian virus 40 transformed newborn human kidney cell cultures were infected with H-1 stock virus, resulting in a marked drop in the rate of incorporation of ³H-thymidine into DNA late in infection. Autoradiographic measurements revealed that the inhibition of total DNA synthesis was due to a decrease in the capacity of an infected cell to synthesize DNA. Thymidine kinase activity increased 1.5- to 2.6-fold during a period of virus maturation (20-48 hr), but, later in infection, it decreased to 11-43% of the control cell activity. A similar decline in enzyme activity was also observed in "Salk monkey heart" cells late after H-1 infection. Extracts prepared from newborn human kidney cells infected for different times had no effect on the enzyme activity from uninfected cells. The decrease in thymidine kinase activity found after H-1 infection relative to control cell activity was apparently dependent on *de novo* protein and DNA-dependent RNA synthesis.

0211 RADIATION-ENHANCED ONCOGENESIS BY SV40. (E.) Coggin, J. H. (Oak Ridge Natl. Lab., Tenn.), S. E. Harwood and N. G. Anderson. *Proc Soc Exp Biol Med* 134(4):1109-1111, 1970.

Hamster and mouse embryo cells exposed to X-irradiation prior to infection with simian virus 40 showed an increased frequency of transformation *in vitro*. Neonatal hamsters were tested for increased sensitivity to simian virus 40 tumorigenicity after exposure to localized, low-level X-ray at the site of virus inoculation *in vivo*. Irradiation of a target area prior to infection markedly decreased the time to tumor appearance and increased the frequency of tumor occurrence. No tumors occurred in irradiated animals that did not receive virus. Although low doses of localized X-ray may have resulted in modest immunologic suppression, this was not a primary factor in tumor enhancement. Tumors appearing in simian virus 40 infected animals uniformly possessed viral neoantigens.

0212 STUDIES ON THE BIOCHEMICAL PROPERTIES OF SURFACE COMPONENT OF NORMAL AND SV-40 TRANSFORMED 3T3 MOUSE CELLS. (E.) Sheinin, R.

(Ontario Cancer Inst., Toronto, Canada) and K. Onodera. *Canad J Biochem* 48(8):851-857, 1970.

Biochemical and biophysical properties of isolated and partially purified (sonication, dialysis, and DEAE-cellulose column chromatography) surface components of 3T3 and SV40-transformed 3T3 mouse cells were examined. The incorporation patterns of various radioactive precursor substances (glucosamine, amino acids, choline, uridine, and thymidine) into the surface component indicated that the components contain carbohydrate and peptide (probably as glycoprotein) but do not contain lipid, RNA, or DNA. Both velocity sedimentation in sucrose density gradients and gel filtration (Sephadex G-200) indicated that the surface molecule is large, and may have a molecular weight of 60,000 Daltons.

0213 REACTION OF SERUM FROM PREGNANT HAMSTERS WITH SURFACE OF CELLS TRANSFORMED BY SV40. (E.) Duff, R. (Coll. Med. U. Pennsylvania, Hershey) and F. Rapp. *J Immun* 105(2):521-523, 1970.

The surface antigen on SV40-transformed Syrian hamster cells was compared to an antigen found during hamster embryonic development. When sera from pregnant hamsters (collected 14-15 days after onset of their second pregnancy) were incubated with cells transformed by SV40 or defective SV40, the majority (>80%) of the pregnant hamster sera reacted specifically with the cell surfaces; no reaction was observed with normal cells. In another experiment, pregnant sera did not react with hamster cells transformed by simian adenovirus 7 or by dimethylbenzanthracene, indicating a definite specificity of the pregnant sera for SV40 transformed cells. The antibody was present in sera of 1 out of 7 hamsters pregnant for the first time, but in 5 of 6 animals pregnant for the second time; 1 week after termination of pregnancy, the antibody was no longer detectable in the hamsters.

0214 THE SUPERINFECTION OF ABORTIVELY INFECTED MONKEY KIDNEY CELLS WITH SV40: BRIEF REPORT. (E.) Sauer, G. (German Cancer Res. Ctr., Heidelberg) and E. C. Hahn. *Arch Ges Virusforsch* 30(2-3):267-270, 1970.

The relation of abortive infection with SV40 and resistance to super-infection was studied in African green monkey kidney cells (GMK) by observing the presence of viral coat protein and tumor-antigen with immunofluorescence. Infection with SV40 (3 plaque forming units (PFU)/cell) produced 17% abortively infected cells and 70% cells with both viral coat protein and tumor-antigen. Superinfection (20 PFU/cell) of cells 24 and 48 hr after the first infection with 3 PFU/cell resulted in 100% of the cells having viral coat protein. The lack of resistance indicates that the incomplete viral information in the abortively infected cell does not affect the susceptibility of these cells to productive superinfection.

0215 POLYOMA VIRUS TRANSFORMATION OF 3 HAMSTER CELL LINES *IN VIVO*: ELECTROPHORETICAL STUDIES. (It.) Fimiani, V. (Fac. Med. U. Perugia,

Italy) and F. Bistoni. *Boll Ist Sieroter Milan* 49(2):164-168, 1970.

Electrophoretic migration of 3 transformed cell lines (B-, G- and F-) originating from an LID-I strain polyoma virus-induced s.c. hamster tumor was compared to migration of normal cells (kidney fibroblasts and red blood cells) obtained from a healthy hamster. A Gittens-James instrument (cells containing a 3.5 M soln of KCl) was used; the applied current was 50 V and 5 mA, and the experiments were performed at room temperature (17-19°C). The 3 transformed cell lines revealed a higher migration rate (higher surface negative charge) than the control cells. The F-cell line presented the highest migration rate of the transformed cell lines; this was attributed to their having the largest number of sialic acid residues on the cell surface. However, no direct relation between membrane sialic acid levels and cell malignancy was established.

0216 REQUIREMENT OF SERUM FOR DNA SYNTHESIS IN BHK 21 CELLS: EFFECTS OF DENSITY, SUSPENSION AND VIRUS TRANSFORMATION. (E.) Clarke, G. D. (Imperial Cancer Res. Fund., London, England), M. G. P. Stoker, A. Ludlow and M. Thornton. *Nature* 227(5260): 798-801, 1970.

The serum requirement of both normal and transformed cells in culture in different conditions of density and anchorage were determined. The BHK 21 hamster cell line (Cl3 clone) and a polyoma virus transformed derivative were grown in Dulbecco's modified Eagle's medium containing 10% calf serum and ³H-thymidine. Layers of resting cells originally seeded at different densities were exposed to increasing serum concentrations; the BHK 21 cells showed density dependent inhibition of DNA synthesis in low concentrations of serum. In virus-transformed cells, the initial response to serum was very high because a large proportion of cells were synthesizing DNA even in 0.2% serum; in over half of the transformed cells, DNA synthesis occurred in the complete absence of serum. With the transformed cells, there was little difference between anchored and suspended cells, whereas in the normal BHK 21 cells, suspended cells were 60 times less sensitive to serum concentration than anchored cells; the latter showed a 3-fold decrease in sensitivity when the density increased 10-fold. The requirement for a serum factor for initiation of DNA synthesis which is necessary for normal cells appears to be removed or greatly reduced in the virus-transformed cells.

0217 ENZYMATIC METHYLATION OF TRANSFER RNA BY EXTRACTS OF POLYOMA VIRUS-TRANSFORMED CELLS. (E.) Breier, B. (Mount Sinai Sch. Med., New York, N. Y.) and R. W. Holley. *Biochim Biophys Acta* 213(2): 365-370, 1970.

Enzymatic methylation of *Escherichia coli* tRNA and rat liver tRNA *in vitro* by extracts of polyoma virus-transformed cells (HPy, 3T3, 3T3Py, BHKPy, and BHK) was studied using ¹⁴C-S-adenosyl-L-methionine (labeled in the methyl group). With *E. coli* tRNA as substrate in the polyoma virus-transformed HPy cell line,

(from hamster) fluctuations occurred in the activities of 5 different tRNA methylases (specific for N²-methylguanine, N¹-methylguanine, N²,N²-dimethylguanine, N¹-methyladenine, and 5-methyluracil) at pH values of 7.2, 8.0, and 8.8, while with rat liver tRNA as substrate only the N¹-methylguanine-specific methylase had any activity (53 cpm) at pH 8.8. The mouse cell line 3T3 and its transformed cell line 3T3Py yielded similar results with the N¹-methylguanine-specific methylase activities (cpm) at 30 and 25, resp., with *E. coli* tRNA at pH 8.8 and at 22 and 62, resp., with rat liver tRNA at the same pH. The BHK cell line of hamster cells and its transformed BHKPy yielded N¹-methylguanine-specific methylase activities of 96 and 115, resp., with *E. coli* tRNA and of 42 and 96, resp., with rat liver tRNA. The hypothesis for a polyoma virus-induced tRNA methylase is not supported.

0218 RNA SYNTHESIS IN POLYOMA VIRUS-INFECTED CELLS: I. PATTERN OF FORMATION OF POLY-RIBOSOME-ASSOCIATED MESSENGER RNA DURING PRODUCTIVE INFECTION. (E.) Cheevers, W. P. (Cancer Res. Lab., U. Western Ontario, London, Canada) and R. Sheinin. *Canad J Biochem* 48(10):1104-1112, 1970.

Secondary cultures of mouse embryo cells were infected with polyoma TSPI virus at an estimated input multiplicity of 1-10 PFU/cell to investigate the pattern of formation of polyribosome-associated mRNA in polyoma-infected mouse embryo cells. It was found that productive infection of these cells by polyoma virus resulted in stimulation of mRNA synthesis; the pattern of induction of mRNA synthesis was biphasic, characterized by distinct early and late periods, as denoted by the time of initiation of progeny viral DNA replication. The formation of early mRNA was first detected at 9-11 hr post-infection, 6 hr prior to the time of onset of virus-induced synthesis of cell DNA and 9 hr prior to initiation of polyoma DNA replication. The initiation of synthesis of late mRNA was approximately coincident with the onset of formation of viral DNA. Most of the newly synthesized "early" and "late" mRNA was of relatively small size (8-12 S) and was associated with polyribosomes which sedimented at less than 180 S. The mRNA which was synthesized both early and late was predominantly cell-specific but the ratio of total late mRNA which was virus-specific was 3 times higher than the ratio of total early mRNA.

0219 PRELIMINARY VIROLOGICAL AND IMMUNOLOGICAL STUDIES OF THE SALIVARY GLAND TUMOR OF C₃H/He MOUSE. (E.) Castelli, L. (Regina Elena Inst. Cancer Res., Rome, Italy) and A. Caputo. *Experimentia* 26(7):780-781, 1970.

An attempt to isolate an agent identical with or similar to polyoma virus from the salivary gland tumor of C₃H mice is described. Polyoma virus particles were not found in tumor cell cultures; and no cytopathic effect was apparent after the addition of cellular suspensions or cell-free tumor extracts of polyoma virus to mouse embryo cell cultures. In addition, when polyoma virus was artificially introduced into the system a slight de-

crease of tumor takes was obtained, confirming that the etiology of this tumor cannot be restricted to polyoma virus. Immunological studies in mice inoculated with homogenized tumor cells followed by challenge with whole tumor cells indicated that the tumor was unable to produce an appreciable immunological response in isogenic hosts.

0220 ISOLATION, ANALYSIS AND RADIOACTIVE LABELING OF NUCLEIC ACIDS OF POLYOMA VIRUS-INDUCED TUMORS IN RATS. (Ger.) Pokorny, J. (Borstel Res. Inst. Germany), E. Fasske, R. Fetting and S. Reth. *Z Krebsforsch* 74(3):219-226, 1970.

Inoculation of a polyoma virus (strain BB/T2, cultured for 6 yr on mouse embryonic cell cultures) into newborn Wistar rats induced the development of 5 histologically different transplantable tumors. The fibrosarcomas and liposarcomas contained AT-type DNA while the other tumor types, adenocarcinomas, solid carcinomas and rhabdomyosarcomas contained the GC-type of DNA; control normal tissues contained mainly GC-type DNA. The number of purine and pyrimidine bases within the tumor transplant strains was constant. Carcinomas originated in the thyroid while rhabdomyosarcomas developed in the skeletal muscle system. Distribution studies with labeled tumor DNA in organs of normal animals revealed the spleen as the main site of DNA accumulation; it is suggested that oncogenic viral DNA may similarly accumulate in the spleen.

0221 DENSONUCLEOSIS VIRUS DNA SYNTHESIS: HIGH RESOLUTION AUTORADIOGRAPHY. (Fr.) Krustak, E. (Fac. Med. U. Montreal, Quebec, Canada). *Rev Canad Biol* 29(2):207-211, 1970.

- * Rev (0002) (0003) (0004) (0005) (0006) (0021)
- * Chem (0076)
- * Immun (0241)
- * Path (0263)

- 0222 TRANSFER OF TUMOR IMMUNITY WITH RIBONUCLEIC ACID. (E.) Pilch, Y. H. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.) and K. P. Ramming. *Cancer* 26(3):630-637, 1970.

Normal C3H mouse spleen cells were incubated with RNA extracted from the lymphoid organs of guinea pigs immunized with a benz(a)pyrene-induced fibrosarcoma to achieve the transfer of antitumor immunoreactivity to normal, nonimmune lymphoid cells. Injections of the immunized cells into normal C3H mice significantly inhibited the development of subsequent isografts of the same tumor. RNA from pigs immunized with normal C3H tissues was ineffective, and RNAase treatment of the RNA preparations removed all activity. Within a completely syngeneic tumor-host system, strain 2 guinea pig spleen cells were incubated with RNA extracted from the spleens of strain 2 guinea pigs previously immunized with a strain 2 guinea pig liposarcoma induced by methylcholanthrene. Immunoreactivity of these cells was demonstrated by their ability to cause areas of specific immune cytolysis in monolayers of methylcholanthrene-induced tumor cells *in vitro*. This reaction was found not to be dependent on the presence of phytohemagglutinin. RNA extracted from the spleens of guinea pigs stimulated nonspecifically by immunization with Freund's adjuvant, but not exposed to the tumor, was ineffective. Normal lymphoid cells, incubated with solubilized extracts of methylcholanthrene-induced tumor tissue known to be rich in tumor-specific transplantation antigens, but containing no RNA, failed to match the RNA preparations in production of immune cytolysis.

- 0223 RADIATION DOSE-INDEPENDENT INACTIVATION OF ISOLOGOUS MOUSE LYMPHOMA CELLS BY NONSPECIFIC RESISTANCE. (E.) Maruyama, Y. (U. Minnesota Hlth. Sci. Ctr., Minneapolis), C. Ceman and R. B. McHugh. *Cancer Res* 30(8):2245-2251, 1970.

The antigenicity of X-irradiated LSA lymphoma of C57BL mice was assessed to determine whether the tumor can be recognized and inactivated by immunologically competent recipient mice. Pretreatment of the recipient mice with X-ray-killed cells at weekly intervals for 3 weeks did not alter the TD₅₀ (cell dose required to produce 50% tumor takes among challenged recipients) so that a conventional tumor antigenicity was not detected. Tumor cells assayed in immunologically suppressed (whole body irradiation of 400 rads) and nonsuppressed recipients revealed significantly different effective fractions (0.39 and 0.13, resp.) indicating that the tumor cells were inactivated by the immune-competent host. A 2-fold increase in cell dose for the nonirradiated mice to compensate for the lower proportion of takes in the nonsuppressed group made it possible to produce comparable proportions of takes in both groups; when X-irradiated cells were assayed using this factor, similar numbers of takes were observed. A weak form of host resistance against tumor cells which reduced tumor cell survival appears to exist; this nonspecific resistance is dose independent, and is effective against small numbers of challenging cells and against single viable cells in a large population of identical nonviable cells.

- 0224 CHRONIC ALLOGENEIC DISEASE: II. DEVELOPMENT OF LYMPHOMAS. (E.) Armstrong, M. Y. K. (Dept. Microbiology, Yale U., New Haven, Conn.), E. Gleichmann, H. Gleichmann, L. Beldotti, J. Andre-Schwartz and R. S. Schwartz. *J Exp Med* 132(3):417-439, 1970.

Inoculation of parental cells (BALB/c spleen) into 371 (BALB/c A/J)F₁ hybrids triggered a sustained immunoproliferative reaction, and at the end of 24 months, a 33% incidence of reticulum cell sarcomas developed, compared to 3% for controls. The development of the neoplasms was a function of the number of parental cells administered. Analyses of the injected mice for the presence of donor cells indicated that the majority of the injected parental cells lost antihost activity, probably within 24 hr of their administration. Transplantation tests and antigenic analysis of tumor cells showed that the tumors were of host origin.

- 0225 ALLOGRAFT SURVIVAL IN NONSUSCEPTIBLE C57BL/6J MICE HOSTS: TEMPORAL RELATIONSHIP BETWEEN WHOLE-BODY X-IRRADIATION AND THE IMMUNE RESPONSE. (E.) Halkett, J. A. E. (Boston VA Hosp., Mass.). *Radiology* 96(3):645-648, 1970.

Female mice, shown to be resistant to transplants of mouse leukemia, were exposed to X-irradiation (400 rads) before or after receiving leukemia cell injections to test allograft survival in irradiated nonsusceptible hosts. Preirradiated mice died of leukemia, but postirradiated mice did not, as confirmed by transfer of homogenized spleens from irradiated allogenic hosts to AKR strain mice syngeneic with the leukemic cells. More leukemic cells developed in preirradiated hosts spleens, a finding which suggests that preirradiation may damage concentration-dependent control mechanism regulating allograft proliferation.

- 0226 POLYPEPTIDE CHAIN STRUCTURE OF IMMUNOGLOBULINS. II. ISOELECTRIC SEPARATION OF NORMAL AND MYELOMA IgG-GLOBULINS AND THEIR POLYPEPTIDES. (Ger.) Reis, H. E. (Clin. Intern. Med., Ruhr U., Essen, Germany), O. Wetter and T. Hake. *Klin Wschr* 48(14):862-866, 1970.

G-type immunoglobulins (IgG) and their light and heavy polypeptide chains from normal and myeloma sera were subjected to isoelectric focusing on a column provided with a combined pH and density gradient. IgG from normal sera separated into several heterogenous components (with multiple fractions) with isoelectric points ranging between pH 5 and pH 9 while IgG from myeloma sera separated into homogenous components (single fractions) with specific isoelectric points in the same range. Similar results were obtained by the fractionation of light and heavy polypeptide chains. While light and heavy chains from normal sera manifested considerable heterogeneity, the ones from myeloma sera appeared homogenous. Polyacrylamide-gel electrophoresis revealed no direct relation between isoelectric points and electrophoretic mobility. Quantitative amino-acid determinations, end group investi-

gations and other physical-chemical techniques revealed that amino acid distribution as well as protein conformation determined the differences of behavior of the light polypeptide chains.

- 0227 IMMUNOLOGY OF TROPHOBLASTIC TUMORS. (E.) Jakoubkova, J. (Oncol. Lab. Charles U., Prague, Czechoslovakia), A. Majsky, E. Ivaskova, M. Zavadil and V. Snajd. *Neoplasma* 17(3):223-229, 1970.

Serological studies were performed on 250 patients with trophoblastic diseases; patients were categorized as having benign trophoblastic disease (including benign trophoblastic invasion and mola hydatidosa) and malignant trophoblastic disease (including mola proliferans and chorioepithelioma). Sera of 69 and 32 women were examined for the presence of platelet and leucocyte antibodies. These antibodies were found in both above mentioned groups and were also present in sera of primiparous women without any transfusion in anamnesis. Platelet antibodies, mostly of the incomplete type, were found in 21 sera, cytotoxic leucocyte antibodies in 17 patients; their incidence in trophoblastic disease in comparison with that in healthy multiparous women was significantly higher. Examination of leucocytes of 15 women and their husbands for HL-A antigens revealed that 12 women were negative and 11 men were positive for the antigen Mac.

- 0228 DELAYED HYPERSENSITIVITY AND NEOPLASIA: *IN VITRO* STUDIES WITH MACROPHAGE MIGRATION. (E.) Steiner, T. (Mayo Grad. Sch. Med., U. Minnesota, Rochester) and A. L. Watne. *Cancer Res* 30(8):2265-2270, 1970.

Delayed hypersensitivity reactions of cells from rats bearing transplantable tumors was studied using an *in vitro* observation of macrophage migration. The reactions of peritoneal cells from tumor-bearing and normal animals were studied in extracts of homologous tumor, normal tissue, and specific antigen. Rats sensitized to tuberculin evidenced inhibition of cell migration when cultured in media containing purified protein derivative, and injection of 1.0, 10.0, or 20.0 million tumor cells s.c. 10 days prior to culture had no effect on this inhibition. Both normal rats and mice and those bearing transplantable tumors showed enhanced cell migrations when cultured in the presence of either normal tissue or pooled homologous tumor extracts. One group of rats were given injections of 1.0×10^6 tumor cells in the hindfoot, and after 10 days these legs were surgically removed. At that time or 2 weeks later, *in vitro* macrophage migrations were examined in the presence of extracts of the rat's own tumor, pooled tumor, and normal tissue. The rats showed enhanced cell migrations in extracts of normal tissue or pooled tumor; in extracts of the rat's tumor only, there was a tendency toward inhibition of cell migration. Tumor-bearing and normal rats evidently do not show any delayed hypersensitivity reaction to extracts of normal tissue or pooled tumor as evidenced by inhibition of macrophage migration *in vitro*. The enhanced cell migration observed in the 2 extracts is probably a non-immunological response.

- 0229 OBSERVATION OF IMMUNOGLOBULINS IN THE COURSE OF A TUMOR DISEASE. (E.) Dostalova, O. (Motol Hosp., Prague, Czechoslovakia), E. Schon, V. Kubelka and F. Holik. *Neoplasma* 17(3):231-240, 1970.

The method of simple radial diffusion in agar was used to examine the blood of 130 patients with breast, bronchial, laryngeal and other carcinomas for the purpose of observing the levels of the IgG, IgA and IgM immunoglobulins in their blood. Immunoglobulin levels were observed to vary in relation to the course of the disease, and in relation to the therapy used. The average levels of IgG and IgM were within the limits determined for the healthy population, while the IgA levels were higher than normal, particularly in patients in an advanced stage of disease. Eighty patients were examined repeatedly, and, in these, values for IgM and IgG were decreased as the course of the tumor disease advanced; in the same group, actinotherapy and cytostatic therapy had a depressing effect on the IgG level, while a stimulating effect on immunoglobulin level was produced by immunotherapy and hormone treatment by Agovirin.

- 0230 *IN VITRO* LYMPHOCYTE STIMULATION BY A SOLUBLE ANTIGEN FROM MALIGNANT MELANOMA. (E.) Nathanson, L. (New England Med. Ctr. Hosp., Boston, Mass.), U. W. Jehn, R. S. Schwartz and M. Skinner. *New Eng J Med* 283(7):329-333, 1970.

A soluble tumor antigen extracted from a cystic neoplasm in a patient with metastatic malignant melanoma was characterized and incubated with lymphocytes of 6 other melanoma patients. The tumor fluid contained an electrophoretic peak corresponding to β -globulin, which was separated from albumin, melanin, and γ -globulins by starch-block electrophoresis. The urine of this patient contained a peak with the same mobility, and gel diffusion studies using antisera to rabbit tumor fluid and urine revealed that both substances were antigenically identical. When tested in autologous lymphocyte cultures, the whole tumor fluid stimulated DNA synthesis; of the electrophoretic fractions only β -globulin fraction also stimulated DNA synthesis. The lymphocytes of the other 6 patients were stimulated when incubated with crude autologous tumor extract and when incubated with the tumor fluid of the first patient, although lymphocytes from normal patients did not respond to either tumor extracts or the tumor fluid.

- 0231 AGE DISTRIBUTION OF α -FETOPROTEIN IN HEPATOCELLULAR CARCINOMA. (E.) Bagshawe, A. (Dept. Med., U. Coll., Nairobi, Kenya) and A. M. Parker. *Lancet* 2(7666):268, 1970.

The influence of age on the occurrence of α -fetoprotein in patients with hepatocellular carcinoma and teratocarcinoma was investigated. α -Fetoprotein was detected in the serum of 15 of 24 patients with primary hepatic carcinoma, and correlation of the presence of α -fetoprotein with the age of the patients indicated that positive tests occurred mainly in younger patients (e.g., those under 30). Observed geographic variations in the occurrence of α -fetoprotein in hepatocellular carcinoma may

reflect the age-incidence of the tumor. Variation in the age at which the tumor occurs may indicate different etiological factors, but these need not directly influence α -fetoprotein production by the tumor.

- 0232 IMMUNOGLOBULIN (IgG, IgA AND IgM) LEVELS IN PRIMARY CARCINOMA OF THE LIVER AND CIRRHOSIS OF THE LIVER IN SINGAPORE. (E.) Chew, B. K. (Dept. Med., U. Singapore), M. Yu and R. Wee. *Med J Aust* 57(1):18-21, 1970.

The sera from 34 patients with carcinoma of the liver and from 36 cirrhotic patients were examined to determine the levels of the immunoglobulins IgG, IgA and IgM by the micro-double-diffusion agar method. In 65% of cases of primary carcinoma of the liver and in 83% of cases of cirrhosis the serum IgG level was elevated. IgA values were raised in 70% of cases of primary carcinoma of the liver and in 78% of cases of cirrhosis of the liver. No change was detected in IgM values, although in most of the cases of primary carcinoma of the liver the IgM values were well below the normal mean. The patterns of immunoglobulin levels in these 2 conditions were almost similar and therefore could not be used as a diagnostic aid.

- 0233 BONE MARROW SMEARS FROM CHILDREN WITH ACUTE LEUCOSIS: IMMUNOFLUORESCENCE MICROSCOPY. (Ger.) Hempel, H. C. (St. Child. Clin., Karl Marx St., Germany), J. Grimm and A. Tier. *Folia Haemat* 93(1):42-50, 1970.

Fluorescence microscopy of bone marrow smears from 12 children (10 with acute leucocytosis and 2 with acute myelosis) was performed on the following preparations: bone marrow smear, leukemic autologous serum and labeled Race-Coombs-serum; bone marrow smear and labeled leukemic autologous serum; and bone marrow smear and labeled Race-Coombs-serum. Control tests were made on bone marrow smears alone, bone marrow smears and dye solution, and bone marrow smears and labeled serum from healthy children. The dye used for serum globulin coupling was fluorescein isothiocyanate (FITC). Sera from the children were treated according to a modification of Coons et al by Koeditz and Wagner. Bone marrow smears of children with leucocytosis revealed a specific indirect fluorescence in 5 cases, a distinct direct specific fluorescence in 3 cases and a slight positive reaction in 2 cases. Positive reactions were obtained in only 1 of the 2 acute myelosis cases; all control tests were negative. Specific inhibition studies are needed to demonstrate the presence of antibodies in sera of patients with acute leukocytosis.

- 0234 CYTOLOGICAL STUDIES OF TUMORS: XLIX. CHRONIC LYMPHOCYTIC LEUKEMIA WITH A₁/G CHROMOSOME TRANSLOCATION AND HIGH SERUM γ -GLOBULIN PRODUCTION. (E.) Obara, Y. (Zool. Inst. Hokkaido U., Japan), S. Makino and C. Mikuni. *Cann* 61(1):1-6, 1970.

A 73-yr-old-male patient, diagnosed as a case of chronic lymphocytic leukemia, was found to have a

presumptive A₁/G translocation and an abnormally high serum γ -globulin content. In the blood culture, under the influence of phytohemagglutinin, mitosis of non-leukemic lymphocytes became predominant over that of leukemic lymphocytes with the A₁/G translocation, while A₁G cells comprised one-half of the metaphase population grown without phytohemagglutinin. At least 3 kinds of lymphocytes were present; leukemic lymphocytes with or without the A₁/G translocation dividing *in vitro* without phytohemagglutinin, and normal lymphocytes proliferating only under phytohemagglutinin stimulation. The amount of serum γ -globulin was extremely high in this patient. Analyses by immunoelectrophoresis and immunoplate revealed a striking increase of IgG. The A₁/G cells in the present case may or may not be related to the elevated γ -globulin production.

- 0235 POSITION OF THE CARCINOEMBRYONIC ANTIGEN OF THE HUMAN DIGESTIVE SYSTEM IN ULTRA-STRUCTURE OF TUMOR CELL SURFACE. (E.) Gold, P. (Montreal Gen. Hosp., Quebec, Canada), J. Krupey and H. Ansari. *J Nat Cancer Inst* 45(2):219-225, 1970.

The ultrastructural position of the carcinoembryonic antigen, a tumor-specific constituent of all adenocarcinomas arising from the endodermally derived epithelium of the digestive system, was localized on the surface of the tumor cell by electron microscopy and use of a ferritin-anticarcinoembryonic antigen conjugate. Normal colonic tissue samples incubated with the ferritin-antibody conjugate revealed no significant ferritin labeling under electron microscopy; in contrast, tumor cells exposed to the ferritin-antibody conjugate showed localization of ferritin primarily in the glycocalyx coating the cell surface membrane. The localization of carcinoembryonic antigen on the cell surface could explain the presence of the antigen in sera and stools of patients with cancer of the large bowel without presupposing the necessity of tumor tissue necrosis and subsequent absorption of released components.

- 0236 EFFECT OF PHYTOHEMAGGLUTININ AND PROSTAGLANDINS ON CYCLIC AMP SYNTHESIS IN RAT LYMPH NODE LYMPHOCYTES. (E.) Novogrodsky, A. (Weizmann Inst. Sci., Rehovot, Israel) and E. Katchalski. *Biochim Biophys Acta* 215(2):291-296, 1970.

The relationship between cyclic AMP and phytohemagglutinin action on lymphocytes was investigated. RNA and DNA synthesis in rat lymph node lymphocytes, both of which are stimulated by phytohemagglutinin, was only slightly enhanced or not affected by 10^{-5} - 10^{-8} M dibutyryl cyclic AMP; higher concentrations (10^{-4} M) were inhibitory. The rate of incorporation of labeled adenine into cyclic AMP in rat lymphocytes was unaltered as a result of incubation with phytohemagglutinin for 30 min. Prostaglandin E₁ markedly stimulated cyclic AMP formation in rat lymphocytes by enhancement of adenyl cyclase, but caused no cell transformations. Phytohemagglutinin (50 μ g/ml) had no effect on adenyl cyclase activity, confirming that rat lymphocyte transformation by phytohemagglutinin is not mediated by cyclic AMP.

37 THE *IN VITRO* TRANSFORMATION OF FROZEN-STORED LYMPHOCYTES IN THE MIXED LYMPHOCYTE REACTION AND IN CULTURE WITH PHYTOHEMAGGLUTININ D SPECIFIC ANTIGENS. (E.) Mardiney, M. R., Jr. (Baltimore Cancer Res. Ctr., Md.) and R. J. Mangi. *Exp Med* 132(3):401-416, 1970.

A study of the *in vitro* transformation of lymphocytes which have been frozen and stored at -60 C indicated that cells frozen at different times and stored for various times do transform in a reproducible manner when placed in culture with phytohemagglutinin, or as one population of the two-way mixed lymphocyte reaction. When frozen-stored lymphocytes are cultured with specific antigen or as both partners in the mixed lymphocyte reaction the response is minimal. The freezing process destroys neutrophils, and the remaining population transforms in a manner similar to cultures of purified lymphocytes. The transformation of frozen-stored human lymphocytes is a practical technique which warrants further investigation and practical application.

38 DNA REPLICATION IN ANTIGEN STIMULATED GUINEA-PIG LYMPH NODE CELLS. (E.) Souleil, (Inst. Pasteur, Paris, France) and J. Panijel. *Nature* 227(5257):456-460, 1970.

A replication was studied in primed guinea pig lymph node cells stimulated *in vitro* by homologous antigen (ovalbumin or hemocyanin) or by phytohemagglutinin. Deoxythymine, a density label which can be incorporated quantitatively into DNA, and ³H-bromodeoxyuridine were also added to the culture medium, and the labeled DNA, which represented the responsive cells, was separated on a CsCl gradient. The banding pattern of fragments of labeled DNA extracted from antigen-stimulated cultures was characterized by a bimodal distribution, but fragments from phytohemagglutinin-stimulated cultures showed only a single peak. Antigenic stimulation appears to trigger an alteration in the sequential replication of DNA corresponding to the series of genes involved in the physiological events underlying antibody synthesis.

39 LYMPHOCYTE TRANSFORMATION IN MALIGNANT LYMPHOMAS. (E.) Papac, R. J. (Yale U. Sch. of Med., New Haven, Conn.). *Cancer* 26 (2):279-286, 1970.

Peripheral blood lymphocyte cultures were established from 19 patients with malignant lymphomas, lymphosarcomas, and Hodgkin's disease to test the capacity of lymphoid neoplasms to respond to phytohemagglutinin; control subjects included both healthy and chronically ill subjects. A wide range of responsiveness to phytohemagglutinin was observed in cases of lymphosarcoma with a median transformation value for the group lower than that of control subjects (48% vs 60%). Correlation of lymphocyte transformation with phytohemagglutinin was noted with histologic type of lymphosarcoma, with duration of disease and with age of the patient. The most marked impairment of transformation generally occurred in patients with small cell lymphosarcoma, in patients

with brief duration of disease and older age groups. There was little correlation between peripheral blood lymphocyte level and percentage transformation with phytohemagglutinin. In patients with reticulum cell sarcoma, phytohemagglutinin stimulation was quite markedly impaired. Lymphocyte cultures from seventeen cases of Hodgkin's disease, which were included for comparison, showed impaired transformation with phytohemagglutinin (22%), which was related to stage of disease and peripheral lymphocyte levels.

0240 HUMAN CANCER-SPECIFIC PROTEINS. (Fr.) Burtin, P. (Inst. Res. Sci. Cancer, Villejuif, France). *Nouv Rev Franc Hemat* 10(3):335-338, 1970.

0241 USE OF U.V. IRRADIATED POLYOMA VIRUS INDUCED TUMOR EXTRACTS IN TUMOR IMMUNOTHERAPY ON HAMSTERS. (Fr.) Bonneau, H. (Reg. Anti-Cancer Ctr., Marseilles, France), G. Cochet, R. Favre and G. Meyer. *Bull Cancer* 57(1):55-68, 1970.

0242 LYMPHOBLASTIC TRANSFORMATIONS INDUCED BY HEMAGGLUTININS FROM *PISUM SATIVUM* L. AND *ERVUM LENS* L.: TRITIATED THYMIDINE INCORPORATION AND ULTRASTRUCTURE. (Fr.) Coulet, M. (C. H. U. Clermont-Ferrand, France), I. Bernard-Griffiths, D. Godeneche, Y. Fonck-Cussac, G. Betail and J. Guillot. *C R Soc Biol* 164(1):117-121, 1970.

0243 DYNAMICS OF HUMAN LYMPHOCYTE DEDIFFERENTIATION INDUCED BY PHYTOHEMAGGLUTININ. I. MICROKINEMATOGRAPHY AND PRELIMINARY DATA. (Fr.) Teixeira-Pinto, A. A. (Fac. Med. Lisbon, Portugal). *C R Soc Biol* 164(1):222-224, 1970.

- * Rev (0008)(0009)
- * Chem (0045)(0053)(0057)(0077)(0079)
- * Viral (0144)(0145)(0147)(0151)(0152)(0153)(0154)(0155)(0156)(0157)(0163)(0165)(0170)(0180)(0186)(0191)(0207)(0209)(0213)(0219)

- 0244 AMELOBLASTOMA: DELINEATION OF EARLY HISTOPATHOLOGIC FEATURES OF NEOPLASIA. (E.) Vickers, R. A. (U. Minnesota Sch. Dent., Minneapolis) and R. J. Gorling. *Cancer* 26(3):699-710, 1970.

Clinicopathologic data and material from 10 patients with cystic jaw lesions that manifested an apparently distinctive altered epithelium were analyzed and compared with published photomicrographs of early ameloblastomas, mural ameloblastoma, and examples of ameloblastoma arising in association with dental cysts. While the 10 specimens had all been considered cystic, 3 histopathologic alterations were consistently observed that delineated them from dental cysts. Histopathologic changes included: hyperchromatism of basal cell nuclei of the epithelium lining the cystic cavities; palisading and polarization of basal cell nuclei of the epithelium lining the cystic cavities; and cytoplasmic vacuolization of basal cells of cystic linings. Cystic lesions manifesting these histologic changes have been associated with ameloblastoma in a high percentage of instances.

- 0245 PAGET'S DISEASE OF THE VULVA -- A CYTOGENIC STUDY OF SKIN FIBROBLASTS, TUMOR CELLS, AND PERIPHERAL BLOOD LEUKOCYTES IN CULTURE. (E.) Mullick, S. (New England Med. Ctr. Hosp., Boston, Mass.), S. Bamford, G. W. Mitchell, Jr. and R. Gilfillan. *Acta Cytol* 14(7):404-410, 1970.

To investigate the hypothetical connection between chromosomal error and the onset of malignancy, cultured leukocytes, skin fibroblasts, and tumor cells from a patient with Paget's disease of the vulva were examined. A late replicating X chromosome in the large size range of the 6-X-12 (C) series was found in 57.5% of the leukocytes, while 66% of the vulvar skin fibroblasts showed a late replicating X chromosome in the small size range. A similar degree of hyperdiploidy between vulvar fibroblasts and tumor cells (19.3%) and skin fibroblasts of the forearm was observed after challenge with SV40 (20%) while striking differences in degree of hypodiploidy were observed in the same cultures (72% in the challenged cells as compared to 20% in the vulvar cells). Positive T antigen values (12.3% at 3 days and 11.6% at 8 days after challenge with SV40) were recorded in fibroblasts, indicating increased susceptibility to transformation of cells from a site distant to the tumor. The positive correlation of hyperdiploidy values found for unchallenged vulvar skin and tumor cells and the challenged fibroblasts from the forearm may indicate the existence of a mechanism within the cell (possibly reflected in the aberrant X) which renders it highly susceptible to transformation in the presence of an oncogenic agent.

- 0246 SERUM ALKALINE PHOSPHATASE AT THE ONSET OF HODGKIN'S DISEASE. (E.) Aisenberg, A. C. (Massachusetts Gen. Hosp., Boston), M. M. Kaplan, S. V. Rieder and J. M. Goldman. *Cancer* 26(2):318-326, 1970.

Serum alkaline phosphatase levels have been studied in 111 patients at the onset of Hodgkin's disease, and a correlation between elevated levels of the enzyme and the stage of the disease is reported. In Stages I and II, 14% of the patients had elevated enzymes, 65% in Stage III, and 87% in Stage IV. In all stages, a high incidence of elevated phosphatase was seen in patients with fever, but not in those with only pruritis, suggesting a different pathogenesis of the 2 complaints. The liver enzyme was elevated in 23/31 patients, it was not possible to state which enzyme was elevated. The majority of hepatic phosphatase increases were felt to be due to hepatic lymphoma, but several cases of a reversible liver isozyme elevation associated with fever and negative open liver biopsy were encountered. Infrequent elevations of bone phosphatase were seen in young patients with localized Stage I and II Hodgkin's disease; this elevation was considered to be a phenomenon of late adolescent bone growth and not due to osseous lymphoma.

- 0247 OCCURRENCE OF EPITHELIAL ATYPIA IN 51 INDIAN VILLAGERS WITH ORAL SUBMUCOUS FIBROSIS. (E.) Pindborg, J. J. (Royal Dental Coll., Copenhagen, Denmark), F. S. Mehta and D. K. Daftary. *Brit J Cancer* 24(2):253-257, 1970.

Biopsies were performed on the oral mucosa of 51 Indian villagers with oral submucous fibrosis to explore the suggested precancerous nature of oral submucous fibrosis. When sections were examined for epithelial atypia, marked atrophy of the epithelium was found in 71.7% of sections, in which the atrophic epithelium showed no rete ridges. The normally unkeratinized buccal mucosa revealed either ortho- or parakeratosis or hyperortho- or hyperparakeratosis in 48.0%. In one patient the histologic examination disclosed a squamous cell carcinoma. In 22.6% of the biopsies an epithelial atypia was found. Features commonly associated with epithelial atypia included irregular epithelial stratification and increased numbers of mitotic figures. The hypothesized premalignant nature of these atypias is supported by the observation of a squamous cell carcinoma developing in an oral mucosa section changed by submucous fibrosis and by the observation that atypia is often found adjacent to carcinomas that develop in patients with submucous fibrosis.

- 0248 CERVICAL CONE BIOPSY ON THE NORMAL-LOOKING CERVIX WITH ABNORMAL CYTOLOGY. (E.) Slabber, C. F. (Dept. Obstet. Gynec., U. Stellenbosch, Union of South Africa) and J. N. De Villiers. *S Afr J Obstet Gynec* 8(1):36-39, 1970.

The incidence of early cervical cancer in patients with an apparently normal cervix, but abnormal cytology, was studied in a series of patients subjected to cervical cone biopsy. In a 3 yr period, cone biopsy showed that 62% of patients with normal-looking cervix and abnormal cytology had early cervical cancer, including the following pathological diagnoses: carcinoma *in situ*, micro-infiltrating carcinoma, and infiltrating carcinoma. No age

group was free of early cancer; however, micro-infiltrating carcinomas generally occurred at a later age than carcinoma *in situ* (average age of 36.4 and 34.7 yr, resp.). Nulliparity did not render patients immune to early cervical cancer.

49 POLYGONAL CRYSTALLINE STRUCTURES IN HUMAN EPENDYMOMA CELLS. (E.) Tani, E. (Kyoto U. Med. Sch., Japan) and T. Ametani. *Acta Neuropath* (4):359-362, 1970.

Electron microscopic examination of human ependymoma cells revealed polygonal crystalline structures which were situated mainly in the lysosomes. These structures, which were clearly distinguishable from the amorphous matrix of the lysosomes, consisted of a regular spacing (150-160 Å) of alternating dense and less dense layers and had one to three axes of linear densities. The individual dense and less dense layers formed a rectilinear array in one crystalline axis, a tetragonal array in two axes, and a hexagonal array in three axes.

50 INVASION OF CARTILAGE BY AN EXPERIMENTAL RAT TUMOR. (E.) Poole, A. R. (Strangeways Res. Lab., Cambridge, England). *Cancer Res* 30(12):2252-2259, 1970.

The Guerin T8 epithelioma was transplanted into female rats for the purpose of studying the *in vivo* invasion of cartilage of the xiphisternum by malignant tumors. Staining of cartilage with toluidine blue was considerably reduced or absent at the edge of the invading tumor. Frequently, matrix staining around chondrocytes close to the tumor was much more intense than that of more remote matrix. This pericellular staining feature was also observed in cartilage from tumor-free animals treated with papain. It was absent from those which received an excess of vitamin A. Appreciable intercellular β -glucuronidase activity was observed in tumor-infiltrated cartilage, but not in normal cartilage. In chondrocytes, this enzyme was normally observed in all cytoplasmic particles (0.2-0.5 μ in diameter). The presence of the established tumor, however, larger stained particles (1.0-2.0 μ in diameter) were frequently observed. The rate of lysosomal staining for acid phosphatase was unchanged in chondrocytes and fibroblasts of cartilage undergoing early tumor infiltration, but was increased in later stages. Inasmuch as β -glucuronidase was present in the matrix ahead of the invading tumor, the results of the study suggest that lysosomal enzymes are present extracellularly in *in vivo* degradation by tumors.

51 A HISTOCHEMICAL STUDY ON THE HISTOGENESIS OF THE MIXED TUMORS OF THE HUMAN SALIVARY GLANDS. (E.) Mira, E. (Inst. Compar. Anat., U. Pavia, Italy) and I. Vidi. *Acta Histochem* 36(2):199-398, 1970.

The histogenesis of 12 neoplasms in the human parotid, submaxillary and minor salivary glands was studied. The homogeneous material contained in the duct-like cavities of the epithelial areas contain neutral epithelial mucins and, in a lesser quantity,

sialomucins and sulphomucins, also of epithelial origin; the intercellular substances of the myxoid and chondroid areas showed the histochemical properties of the connective tissue mucopolysaccharides, hyaluronic acid and chondroitin sulfate 4 and/or 6. In particular, histochemical evidence suggests that the intercellular substance of the myxoid and chondroid areas of the mixed tumors is of a connective nature, and contrasts with the hypothesis of their production by epithelial or myoepithelial neoplastic cells.

0252 CELL SURFACE COATINGS AND MEMBRANE POTENTIALS OF MALIGNANT AND NONMALIGNANT CELLS. (E.) Hause, L. L. (Marquette Sch. Med., Milwaukee, Wisc.), R. A. Patillo, A. Sances, Jr. and R. F. Mattingly. *Science* 169(3945):601-603, 1970.

Single cells from malignant and non-malignant cell cultures were impaled with microelectrodes for bioelectrical recordings of the electrically charged sialomucin cell coating. Positive electrical prepotentials, which ranged from 1-8 mv which increased with the pH of the cell, were recorded in all malignant cells studied. Normal human trophoblasts and lymphocytes also exhibited positive prepotentials, whereas other normal cells studied rarely gave prepotential readings. The finding of a prepotential associated with a surface constituent of malignant cells suggests the presence of a cell surface coating of an ionic nature.

0253 INVASIVE TUMOR GROWTH: COMPARATIVE HISTOLOGY AND ELECTRON MICROSCOPY, HISTOCHEMISTRY AND BIOCHEMISTRY. VI. HISTOCHEMICAL STUDIES OF BRAIN MYELIN SHEATH LIPIDS DURING TUMOR INFILTRATION. (Ger.) Rath, F. W. (Path. Inst. Martin Luther U., Wittenberg, Germany), U. Bonk, C. Coutelle, R. Coutelle, D. Felicetti and F. Traub. *Acta Histochem* 36(1):64-73, 1970.

Invasive tumor infiltration was studied in 82 brain tumors in mice induced by inoculation of Ehrlich ascites carcinoma. Medullary infiltration began along the capillaries; tumor cell expansion continued within the medulla, gradually dividing the medullary substance into stripes and islets; medullary lipids were still detectable within the tumor cell. Sudden solubilization of sheath fragments between the tumor cells occurred later, and fatty traces resulting from myelin breakdown were barely detectable. Final medullary breakdown within the tumor occurred in the immediate vicinity or within necrotic areas, which were characterized by high levels of unsaturated hydrophobic lipids and cholesterol esters and were considered to be the main source of hydrolytic enzymes. Visible myelin breakdown occurred within the marginal tumor zones, while the tumor cells remained unaltered.

0254 CHROMOSOMES OF ADENOCARCINOMA OF THE CERVIX UTERI WITH A RING AND A MINUTE MARKER CHROMOSOME. (E.) Salimi, R. (Johns Hopkins U. Sch. Med., Baltimore, Md.) and H. W. Jones, Jr. *J Surg Oncol* 2(1):17-22, 1970.

Biopsy studies of the chromosomes of an adenocarcinoma of the cervix uteri were performed by a direct squash method, with the result that a modal number of about 40 chromosomes was obtained from the differentiated portion of the tumor. A ring chromosome and a minute chromosome were seen in 58% of the hypodiploid cells. The undifferentiated part of the tumor showed marked anaplastic activity and hyperchromatism with large heavily stained and multiple nuclei with chromatin condensation and clumping, but with little evidence of mitosis; no successful chromosome preparations could be made from this portion of the tumor.

0255 THE NATURE OF PARTICULATE THYROID PROTEINS IN AN EXPERIMENTAL RAT THYROID TUMOR. (E.)

Salabe, G. B. (2nd. Med. Clin., U. Rome, Italy) and J. Robbins. *Biochim Biophys Acta* 214(1):198-206, 1970.

The nature of microsomal particulate proteins labeled with ^{14}C -leucine or ^{125}I in an experimental rat thyroid tumor able to incorporate ^{125}I into soluble thyroglobulin was investigated. A large proportion (20-50%) of the radioactivity, either ^{14}C or ^{125}I , was particulate and associated with the nuclear or microsomal pellets. When proteins released by deoxycholate from microsomes were analyzed by density gradient centrifugation and tested with a rabbit anti-rat thyroglobulin serum, 60% of the proteins labeled with ^{125}I and 30% of those labeled with ^{14}C had a sedimentation rate of 12 S; the latter reacted with anti-thyroglobulin serum. Density gradient centrifugation patterns of soluble proteins labeled with ^{14}C or ^{125}I for 30 min-18 hr showed that ^{125}I is incorporated into 19-S thyroglobulin, whereas no more than 10% of ^{14}C -leucine was found in the 19-S protein. The remaining 80-90% of the radioactivity had a sedimentation rate of 3-8 S. Microsomes of rat thyroid tumor appear to contain a large proportion of thyroglobulin or its precursors; a deficiency in the mechanism for release of protein from the endoplasmic reticulum may account for the minimal presence or absence of soluble thyroglobulin.

0256 TURNOVER OF MAMMALIAN PHOSPHOLIPIDS: STABLE AND UNSTABLE COMPONENTS IN NEOPLASTIC

MAST CELLS. (E.) Pasternak, C. A. (Dept. Biochem., U. Oxford, England) and J. J. M. Bergeron. *Biochem J* 119(3):473-480, 1970.

Exponentially growing or static neoplastic mast cell cultures were labeled with ^{14}C -choline and ^{14}C -inositol to investigate the phospholipid turnover process; protein and DNA turnovers were also monitored with ^{14}C -valine and ^{14}C -thymidine. Phospholipid turnover followed a biphasic pattern, the unstable rapidly turning-over component accounting for 60-80% of labeled phospholipid. The residual stable component did not turn over any more than did protein or DNA. Subcellular fractions and surface membranes of choline-labeled neoplastic cells contained the same proportion of stable and unstable components as did whole cells. The unstable component was largely phosphatidylcholine; the stable

component was relatively richer in sphingomyelin. There appears to exist 2 classes of phospholipids in neoplastic mast cells, one of which is metabolically stable, and the other which is subject to continual enzyme degradation and resynthesis; the turnover of the unstable component is apparently independent of cell growth, since the rate of incorporation of label was the same for the exponential and stationary phase cells.

0257 CYTOCHEMICAL DEMONSTRATION OF ACID PHOSPHATASE AND NON-SPECIFIC ESTERASES AS A MEANS OF IDENTIFICATION AND ESTIMATION OF DIFFERENTIATION OF HUMAN LYMPH NODE CELLS. (E.) Pruska-Koepe, H. (Med. Acad. Lodz, Poland). *Folia Histochem Cytochem* 8(2):159-176, 1970.

Fifteen human lymph nodes were examined, 3 of which were affected by hyperplastic diseases including lymphoblastoma, reticulosarcoma and lymphogranulomatosis maligna; the activity of acid phosphatase and non-specific esterase in these tissues was studied histochemically. A strong activity of both enzymes was present in reticuloendothelial cells, but absent from lymphatic cells. In malignant hyperplastic diseases of the lymph nodes the number of the reticular cells of the youngest and intensely non-specific esterase-positive generations markedly increased. In lymphoproliferative diseases the type of cells subject to neoplastic transformation affects the enzymatic activity of reticulo-endothelial cells.

0258 PLASMA MEMBRANES: THEIR ATPASE ACTIVITY AND ROLE IN CARCINOGENIC MECHANISM. (E.)

Raikhlin, N. T. (Acad. Med. Sci., Moscow, USSR). *Folia Histochem Cytochem* 8(2):117-120, 1970.

ATPase activity and its localization were investigated in an electron microscopic and histochemical study of the plasma membranes of liver parenchyma cells of normal and hepatoma-bearing adult mice. In the plasma membrane of a neoplastic cell there was either disappearance or a striking suppression of the functional heterogeneity of different membrane regions. The heterogeneity was demonstrable in the normal liver parenchyma cell subjected to the histochemical reaction for ATPase activity. Weakening and, in individual regions, loss of the ability to derive energy from ATP was observed in neoplastic cells. A change in the nature of energy production on the neoplastic cell surface may underlie many manifestations of specific traits of the neoplastic cell, and may be either the cause or a result of a shift in functional interrelationships of subcellular structures.

0259 ELECTRON MICROSCOPIC STUDIES OF THE ATPASE ACTIVITY IN THE NUCLEI OF NEOPLASTIC AND NORMAL LIVER PARENCHYMA CELLS OF MAN AND OF EXPERIMENTAL ANIMALS. (E.) Raikhlin, N. T. (Acad. Med. Sci. USSR, Moscow) and A. S. Shubin. *Folia Histochem Cytochem* 8(2):121-128, 1970.

Transplantable mouse hepatomas and normal mouse liver were examined by electron microscopy to investigate

the localization of ATPase in the nuclei of normal and neoplastic cells. ATPase was localized in all the main structural components of the interphasic nucleus: nucleolus, interchromatinic granules, chromatin, and nuclear membrane. However, the localization of the enzyme in normal cells was somewhat different from that in neoplastic ones: in the nuclear membranes of the latter (in the given experimental conditions) ATPase was almost non-demonstrable. However, the nuclear membrane of the neoplastic cells had lost ATPase, or was unable to manifest its activity in the given experimental conditions, perhaps because of the demonstrated different capacities of the nuclear membranes of normal and neoplastic cells to hydrolyse ATP and consequently to release the energy in this compound on the nuclear surface; this difference may underlie considerable differences in the structural-functional organization of the nuclei and in nucleo-cytoplasmic interactions in the cell types. The nuclear chromatin-bound ATPase of the cancer cell appears to differ in some properties from the earlier recognized ATPases A and B. Furthermore, it may be that ATPase in any structural component of the nucleus changes independently of its localization in other nuclear regions, this being indicative of a certain autonomy in cancer cells. Cancer cells from human liver are approximately identical to cancer cells from experimental animals' liver with respect to nuclear localization of ATPase.

60 AGE DIFFERENCES IN THE HISTOLOGY OF HODGKIN'S DISEASE. (E.) Newell, G. R. Tulane Sch. Publ. Hlth. Trop. Med., New Orleans, La., S. R. Cole, O. S. Miettinen and B. MacMahon. *Nat Cancer Inst* 45(2):311-317, 1970.

ix histologic features of Hodgkin's disease (eosinophilia, atypical mitoses, areas of preserved architecture, extent of disease, Reed-Sternberg cells and extent of fibrosis) reviewed for 284 cases were rated according to severity between 0 and 4; discriminant function score calculated for these features was found to differ strikingly between patients aged 15-35 yr and those aged above 50 yr. Patients with scores less than 5 comprised only 4% of those aged 15-34 yr, but 32% of those aged over 50 yr; the percentages of scores above 15 were 49% and 8%, resp. The distribution of scores for the 15-34 yr age group were 26% for scores under 5 and 74% for scores over 15. The relationship of individual histologic features to a representative series of patients of all ages suggest that at least 2 etiologic entities might be distinguished on the basis of age of onset, 15-34 yr or over 50 yr. Patients in the age group 35-49 yr are probably a mixture of the histologic types comprising the other 2 age groups.

61 POORLY DIFFERENTIATED SUBENDOTHELIAL CELLS IN SWINE AORTAS. (E.) Lee, K. T. (Albany Med. Coll., N. Y.), K. J. Lee, S. K. Lee, H. Imai and M. O'Neal. *Exp Molec Path* 13(1):118-129, 1970.

Eleven pigs maintained for 3 days on a hyperlipemic diet were sacrificed, and the poorly differentiated masses of smooth-muscle cells in the intima of their aorta

induced by this diet were examined by electron microscopy. Because of the location of these lesions in the intima, it was possible that a special subpopulation of subendothelial cells was the origin of the cell masses. A study of 385 poorly differentiated cells lying in the intima of the aortic trifurcation of swine revealed that most of these cells were in close apposition to the endothelium, and that their incidence was approximately 7/100 endothelial cells. By using subjective morphologic criteria, the cells were divided into 3 groups: smooth-muscle cell-like, 30%; monocyte-like, 40%; and unclassified, consisting of cells without specialized features, 30%. The hyperlipemic diet produced no effect on the frequency and fine structure of these cells.

0262 CYTOLOGIC DIAGNOSIS OF MAMMARY TUMORS FROM ASPIRATION BIOPSY SMEARS: COMPARISON OF CYTOLOGIC AND HISTOLOGIC FINDINGS IN 2,111 LESIONS AND DIAGNOSTIC USE OF CYTOPHOTOMETRY. (E.) Zajicek, J. (Karolinska Hosp., Stockholm, Sweden), T. Caspersson, P. Jakobsson, J. Kudynowski, J. Linsk and M. Us-Krasovec. *Acta Cytol* 14(7):370-376, 1970.

0263 THE "CROWN-GALL": AN EXPERIMENTAL MODEL FOR THE MECHANISM OF TUMORIGENIC TRANSFORMATION. (Fr.) Guille, E. (Fac. Sci. Essone, France) and F. Quetier. *C R Acad Sci* 270(26):3307-3310, 1970.

- * Rev (0019)
- * Chem (0025) (0030) (0037) (0051) (0052) (0061) (0081) (0085) (0097) (0098) (0102)
- * Phys (0130)
- * Immun (0242) (0243)
- * Epid-Biom (0293)
- * Misc (0341)

- 0264 AGE-ADJUSTMENT OF INCIDENCE RATES IN CANCER EPIDEMIOLOGY. (E.) Hakama, M. (Finnish Cancer Registry, Helsinki). *Acta Path Microbiol Scand* (suppl. 213):1-47, 1970.

The most useful comparisons of disease frequency in different areas and in different population groups are made by incidence rates of the disease. These rates have been adjusted in order to eliminate the confounding effects of concomitant variables, the most common of which is age. A parametric statistical method age-adjustment is proposed and the biological basis of this procedure in the case of cancerous diseases is outlined. It is proposed that the Gaussian curve approximates the incidence curve for which the age specific incidence rates are discrete estimates. The information included in the specific rates cannot be replaced by a single index. The proposal that the probability of occurrence of a tumor by a given age has a normal distribution leads to 3 indices, maximum value, mean and standard deviation of the incidence curve, which specify cancer incidence by age. The parametric method is applied to 4 different primary sites of cancer: stomach, lung, nervous system, and breast. The proposed method of adjustment applies only in cancerous diseases with age as the confounding variable.

- 0265 EPIDEMIOLOGICAL CHARACTERISTICS OF BREAST CANCER IN MIDDLE AND LATE AGE. (E.) Hems, G. (U. Med. Building, Foresterhill, Aberdeen, Scotland). *Brit J Cancer* 24(2):226-234, 1970.

Data for different countries were examined for associations between breast cancer rates at 40-44 yr and at 65-69 yr with diet, parity, birth rate and blood group, with the result that a positive correlation between breast cancer and sugar and fat intakes was found. The correlation explained three-quarters of the variation in the "late rate" (65-69 yrs), for 22 countries, but only half of the variation in the "early rate" (40-44 yrs). The late rate was, further, positively correlated with estimates of the percentage of nulliparous women (9 populations) and, together with terms for sugar and fat intakes, the multiple regression explained 90% of the variation. Early registration rates (13 populations) were positively correlated with blood group A which appeared, from the multiple regression equation, to contribute more than twice the amount to the early rate than did sugar and fat intakes. The contribution of blood group A to the late rate appeared to be only one-third of that for sugar and fat intakes. The results may indicate that the late breast cancer rate was influenced by environmental factors of food and diet and by factors associated with childbirth, whereas the crucial factor influencing the early rate was a constitutional factor, blood group A.

- 0266 MULTIPLE MYELOMA: A COMMUNITY CLUSTER. (E.) Kyle, R. A. (Mayo Clin., Rochester, Minn.), L. Herber, B. L. Evatt and C. W. Heath, Jr. *JAMA* 213(8):1339-1341, 1970.

Six cases of multiple myeloma were diagnosed among residents of Thief River Falls, Minnesota (popula-

tion 7,151) during 1968. This is a rate of 84 per 100,000, as compared with an expected rate of about 3 per 100,000. The clinical and laboratory features of these cases were typical of myeloma; in addition one case of Waldenström's macroglobulinemia was found during this period. The incidence of other forms of leukemia and lymphoma and of congenital malformation was not increased in the town during the years 1960 through 1968. None of the 6 myeloma patients shared a common association apart from their residence in the same town. The cause of this apparent community cluster of multiple myeloma cases remains obscure.

- 0267 GEOGRAPHIC ASPECTS OF MALIGNANT LYMPHOMA AND MULTIPLE MYELOMA: SELECT COMPARISONS INVOLVING JAPAN, ENGLAND, AND THE UNITED STATES. (E.) Anderson, R. E. (U. New Mexico Sch. Med., Albuquerque), K. Ishida, Y. Ii, T. Ishimaru and H. Nishiyama. *Ame J Path* 61(1):85-97, 1970.

Application of Western diagnostic technics to Japanese case material for reticulum cell sarcoma, lymphosarcoma and Hodgkin's disease indicate that only some of the differences between the relative prevalence of these conditions in Japan and in the United States and England can be explained by discrepancies in classification and/or histologic interpretation. Reticulum cell sarcoma is the most prevalent form of malignant lymphoma in Japan with a relative frequency (42%) that approaches Hodgkin's disease in Western series (49%). Conversely Hodgkin's disease is the least frequently encountered form of lymphoma in Japan with a relative frequency (20%) not far removed from reticulum cell sarcoma (11%) in the West. There is little difference in relative prevalence of lymphosarcoma in Japanese and Western experience. Finally, each type of lymphoma in Japan appears to be associated with a shorter estimated clinical course than the comparable disease in the United States. Discrepancies in host reactivity, which are probably genetically governed, may account for those geographic differences in prevalence of malignant lymphomas.

- 0268 EPIDEMIOLOGY OF PRIMARY MALIGNANT MESOTHELIAL TUMORS IN CANADA. (E.) McDonald, A. D. (Dept. Epidem. Hlth., McGill U., Montreal, Quebec, Canada), A. Harper, O. A. El Attar and J. C. McDonald. *Cancer* 26(4):914-919, 1970.

A compilation made of all fatal malignant mesotheliomas reported in Canada between 1959-1968 revealed 165 tumors, 66% of which occurred in males. Sites of mesothelial malignancy location included the pleura, peritoneum and pericardium. Occupational and residential histories were obtained "blind" from relatives and friends of 90% of the cases and 2 matched control series. An association with definite or probable occupational exposure to asbestos was clearly demonstrated in 20% of the male cases and one female case. Almost all the excess was in the manufacture and industrial application of asbestos rather than in mining or milling. This result suggests that chrysotile is less associated with mesothelial tumors than other forms of asbestos, or that some other factor is also required for

s carcinogenic effects. No association was found with lesser degrees of occupational exposure or residence in asbestos and mining areas, but there was a small excess of possible domestic exposures. The smoking histories in the mesothelial tumor and main control groups were almost identical and unlike those for cases of primary lung cancer. In 9 cases of mesothelial tumor, an occupational exposure to copper, nickel, rubber, or fiberglass was noted.

59 THE EPIDEMIOLOGY OF SKIN CANCER IN QUEENSLAND: THE INFLUENCE OF PHENOTYPE AND ENVIRONMENT. (E.) Silverstone, H. (U. Queensland Med. Sch., Brisbane, Australia) and J. H. A. Searle. *Int J Cancer* 24(2):235-252, 1970.

A multivariate statistical analysis was performed on data on residents of 3 separate areas of Queensland, Australia, to determine the influence of age, sex, susceptibility to sunburn, complexion, eye color, ancestry, occupation, clothing habits and residential area on the etiology of skin cancer and solar keratoses. For both sexes, both diseases and all age groups the susceptibility to sunburn factor proved to be the most important single factor, once the age effect had been removed. On the whole it appeared that the genetically based factors as a group provided more information on susceptibility than the environmental factors. The relative importance of "occupation" remains in some doubt; in the tropical area away from the coast it appears to be of considerable importance, whereas in coastal areas its influence appears to be blunted, presumably by factors such as outdoor sports and recreation habits, which increase the exposure to sunlight of outdoor workers.

70 ON THE FREQUENCY OF LEUKEMIAS AND RELATED DISEASES: AN EVALUATION OF THE BAVARIAN VITAL STATISTICS: 1932-1964. (Ger.) Ambs, E. (Child. Clin., Wurzburg, Germany) and E. Jansen. *Munchen Med Wschr* 112(32):1453-1465, 1970.

An examination of the figures on mortality from leukemia and aleukemia as well as other neoplasms of the lymphatic and hematopoietic organs in Bavaria compiled between 1932-1964 revealed that the incidence of leukemia has increased slightly among persons between 1-5 yr old. However, a clear-cut increase was conspicuous only in age groups from 45-50 yr, and the older the patients, the more increased of leukemia. The rapid increase in leukemia mortality in the elderly is apparently due to an increase in leukemia incidence, rather than to an increase in the proportion of older people. Males showed a higher mortality from leukemia than females, a tendency which became more marked with increasing age.

71 SOME EPIDEMIOLOGICAL FEATURES OF HODGKIN'S DISEASE IN JAPAN. (E.) Nishiyama, H. (Nagoya Cancer Ctr. Res. Inst., Nagoya, Japan) and T. Sue. *Gann* 61(3):197-205, 1970.

A analysis of the mortality rates of age-specific groups, for Hodgkin's disease in Japan, showed a

distinct difference in the 2 age groups observed. Decreasing mortality rates in the young and increasing rates in the elderly with a minor difference in the changing pattern between the sexes were seen. Male predominance was the expected finding through all age groups, while pronounced death rates in the young was not a feature in Japan, and no bimodal curve was observed by examining age distribution in cases dying from Hodgkin's disease. Male-to-female mortality ratios appeared consistently similar in all age groups through 2 different study periods of 1950-58 and of 1959-66. There are marked variations in mortality rates for the 9 districts of Japan, and these seem not to be derived from the difference of diagnostic criteria in each district. The low rate of mortality in large cities like Tokyo and Osaka was unexpected and has not been reported previously.

0272 THE GEOGRAPHICAL DISTRIBUTION OF HODGKIN'S DISEASE AND ITS URBAN/RURAL RATIO IN NORTHERN GERMANY. (Ger.) Dorken, H. (1st Med. U. Clin. Hamburg, Germany), R. Fliessbach and H. Buss. *Z Krebsforsch* 74(2):190-199, 1970.

Between 1964 and 1965, 344 deaths from Hodgkin's disease were recorded in Northern Germany. The age-adjusted death rates of 2.2 per 100,000 inhabitants per year (male) and 1.6 (female) in Hamburg were similar to the known values of other European countries. The rates for Schleswig-Holstein and Niedersachsen, however, were somewhat lower (1.6-1.2 and 1.6-1.4), probably due to failure to diagnose correctly cases in the higher age-groups in these predominantly rural districts. The range of the death rates in the 101 counties investigated (from 0.0 to 7.0 per 100,000 per year) could easily be accounted for by chance variation for relatively small numbers. No evidence of clustering of cases in time and space was seen. Age-adjusted death rates from Hodgkin's disease were approximately equal in urban and rural districts in Northern Germany in both sexes, in contrast to nearly all other neoplasms. However, detailed analysis of age-specific rates showed a slightly higher rate for younger males in rural areas, suggesting the existence of exogenous factors in the rural environment (occupation or animal contacts).

0273 SOFT PART SARCOMAS IN NEGROES. (E.) Leffall, LaS. D., Jr. (Freedmen's Hosp., Washington, D. C.), M. Crawford, E. B. Chung and J. E. White. *Cancer* 26(3):503-512, 1970.

The incidence and pathological distribution of soft somatic tissue sarcomas were studied in 59 Negro patients; sarcomas were classified as: angiosarcoma; extraosseous chondrosarcoma; dermatofibrosarcoma protuberans; fibromatoses (extra-abdominal desmoids); abdominal desmoids; fibrosarcoma; liposarcoma; leiomyosarcoma; myxosarcoma; malignant neurilemmoma; rhabdomyosarcoma, and synovial sarcoma. Fibrosarcoma and dermatofibrosarcoma protuberans were observed in 52% of the patients, with the lower extremity being involved most often (24 patients). Females predominated with a sex ratio of 2:1; associated incidental findings were essen-

tial hypertension (34%) and diabetes mellitus (12%). Blood borne metastases were most frequent, but lymph node metastases also occurred. Angiography was of adjunctive value in 2 patients. Biopsy (incisional or excisional) and treatment by wide local excision, muscle group excision, or amputation were mainstays in management. With exception of desmoids and dermatofibrosarcoma protuberans, 5-yr survival was quite low. Negroes appeared to have a greater number of fibrous tissue tumors than other populations studied.

- 0274 REAPPRAISAL OF BASAL CELL CARCINOMA OF THE EYELIDS. (E.) Blodi, F. C. (U. Hosp., Iowa City, Iowa) and A. L. Aurora. *Amer J Ophthalmol* 70(3):329-336, 1970.

A survey of 172 cases of basal cell carcinoma of the eyelids revealed that the "solid" morphologic type of carcinoma made up 68% of cases, and that this type had an incidence in males twice as high as its incidence in females, whereas the adenoid variety of tumor occurred more often in females than in males. Below the age of 50 yr, basal cell carcinoma of the eyelids seemed to be distributed evenly between men and women; thereafter, however, many more males were affected than females. In females, the condition is apt to have its onset from 6-10 yr earlier than in males, although there is apparently no notable difference in duration of symptoms in the 2 sexes. Circumscribed lesions were more frequent in the lower eyelids, while extensive lesions more often affected the inner canthus. Data on cause of death were available for 68 patients; of these, 9/13 died of malignant diseases other than basal cell carcinoma.

- 0275 SEX MORTALITY RATIOS IN LEUKEMIA. (E.) Nishiyama, H. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan). *Cann* 61(3):263-266, 1970.

The changing patterns of sex mortality ratios for leukemia observed between 1947 and 1966 in Japan are presented. As in the United States and the United Kingdom, a male predominance of leukemia mortality was found for all ages and was most marked in those over 55 yr. Sex mortality ratios decreased in all age groups in Japan during the study period. The predominant type of leukemia among the Japanese is acute granulocytic leukemia, whereas chronic lymphocytic leukemia predominates in Europe. In Japanese leukemia victims over 75-yr-old, the mortality ratio for men is more than twice that for women. This variance may be associated with the fact that elderly Japanese women are more likely than men to be confined to their homes and therefore incur less risk of exposure to leukemia. An increasing rate of female employment in Japan may result in a decrease of male predominance in death rates among the over 55 age group.

- 0276 AN EPIDEMIOLOGIC STUDY OF AN OIL MIST EXPOSURE. (E.) Goldstein, D. H. (New York U. Med. Ctr., New York), J. N. Benoit and H. A. Tyroler. *Arch Environ Hlth* 21(5):600-603, 1970.

A fifteen year mortality study was performed on a group of newspaper pressmen who were occupationally

exposed to a mineral oil mist, and on a control group of compositors who were not so exposed. Although animal experiments have produced lipid granulomas in dogs exposed to petroleum base mineral oil, no significant difference in respiratory mortality or morbidity was encountered. This was supported by particle size determinations which showed more than 85% of the oil droplets were collected by a sampler which showed a 50% cut at 3.5 μ aerodynamic diameter. The respirable fraction was less than 5 mg/cu m. The control group of compositors showed a higher incidence rate of pulmonary carcinomas than the test group.

- 0277 COMPARISON OF AGE, SEX AND INCIDENCE RATES IN HUMAN AND CANINE BREAST CANCER. (E.) Schneider, R. (California St. Dept. Publ. Hlth., Berkeley). *Cancer* 26(2):419-426, 1970.

Since the essential ovarian and anterior pituitary hormones function in a similar manner in the reproductive cycle of man and dog (whereas spontaneous ovulation does not occur in the mouse and rat), a comparison of a 5-yr collection of cases of human breast cancer in males and females from the Alameda County Tumor Registry and a 5-yr collection of canine cases from the Alameda-Contra Costa Counties Animal Neoplasm Registry was made to determine if the pattern of the disease was the same in both. When ages of dogs were converted to human equivalents and canine and human incidence were adjusted to the same population distribution, canine age-adjusted incidence rates were 3 times higher in females and 16 times higher in males. Female age-specific rates increased at the same magnitude for both species until the start of the ages of natural menopause in women; then the human rates continued to increase more slowly, while the canine rates continued to increase at approximately the same exponential value as in the younger age group. A sparing effect on mammary cancer risk for bitches neutered before the age of 2½ yr and a similar decrease in breast cancer risk in women undergoing artificial menopause under 40 yr suggest that enough similarity may exist between man and dog to gain useful information about the etiology of breast cancer from study of dogs.

- 0278 SPACE-TIME CLUSTERING OF CHILDHOOD LEUKEMIA IN SAN FRANCISCO. (E.) Klauber, M. R. (U. Utah Coll. Med., Salt Lake City) and P. Mustacchi. *Cancer Res* 30(7):1969-1973, 1970.

The hypothesis that the incidence of leukemia clusters in space and time was tested by the application of Mantel's regression approach to the records of time of diagnosis and address of 149 leukemia cases diagnosed in San Francisco between 1946 and 1965. The cases were partitioned into consecutive time intervals, and the sum of the distances between pairs of cases falling within intervals was compared to its expectation, assuming a random allocation of space points to time points. Five different interval sizes were used: 0.5, 1, 2, 4, and 12 months. The 2-month intervals were chosen in advance for significance testing purposes at the 5% level. Separate analyses were performed for

ages 0 to 14 and 2 to 14 years. Neither of the age groupings showed statistically significant clustering for 2-month intervals. The only analysis of this same type yielding a p value less than 0.05 was for ages 2 to 14 years and with 12-month intervals ($p = 0.024$). A comparison of "within" time interval average distance between cases to "between" time interval average distance indicated that "clustering" in the series was weak. A single analysis of a case series with a long time span appears to be subject to artifactual space-time clustering occurring in the population at risk.

0279 CANCER STATISTICS, 1970. (E.) Silverberg, E. (Amer. Cancer Soc., New York, N. Y.) and R. N. Grant. *CA* 20(1):10-23, 1970.

Mortality statistics, morbidity statistics, and survival rates related to cancer in the United States show that cancer is the second leading cause of death in the nation (720,892 deaths in 1967), with crude mortality from cancer of the lung and pancreas and from leukemia having increased steadily in both sexes since 1930 (from 2.5 to 42 male deaths per 100,000 population for lung cancer). Mortality from uterine cancer has decreased in females (from 27 to 11 deaths per 100,000 population), and mortality from cancer of the stomach and liver has decreased in both sexes. The increase in mortality from cancer of the pancreas and from leukemia has been slow, while the increase in mortality from lung cancer has been rapid. Morbidity statistics indicate that of 525,000 new cancer cases in the United States, skin cancer (112,000 new cases), lung cancer (68,000 new cases), cancer of the colon (54,000 new cases), and cancer of the prostate (35,000 new cases) are among the most common diagnoses. Survival rates show that lip cancer and thyroid cancer have the highest survival rates (88 and 70% in all stages of disease, resp., for males), leukemia and cancer of the liver the lowest (5 and 2%, in all stages of disease, resp., for females.)

0280 CANCER MORTALITY IN RELATION TO NATIONAL CONSUMPTION OF CIGARETTES, SOLID FUEL, TEA, AND COFFEE. (E.) Stocks, P. (Colwyn Bay, Wales). *Brit J Cancer* 24(2):215-225, 1970.

Age-adjusted death rates from cancers of varying sites in 1964-1965 were compared to figures for annual consumption of cigarettes, solid fuel, tea, and coffee collected from trade statistics in 20 countries. One significant correlation found was that cigarette consumption per adult in the population is positively related with lung and bladder cancer in males and insignificantly with lung in females. Negative relations are indicated with the liver and biliary passages, prostate and uterus. Solid fuel is positively related with the intestine, lung and bladder in both sexes, with leukemia in males and with breast in females; however, negative associations are indicated with the stomach. Tea is positively related with intestine except rectum in both sexes and with larynx, lung and breast in females. Negative associations are indicated with the stomach in both sexes and with uterus and leukemia in females. Coffee is positively

related with the pancreas, prostate and leukemia in males and with ovary and leukemia in females. The contrasts observed between the intestine and stomach in their associations with solid fuel, cigarettes and tea may be explained by the susceptibility of a limited proportion of people at a given age to gastrointestinal cancer and an associated tendency of some carcinogens including those in cigarettes and coal to promote malignancy in the intestines; thus, more intestinal cancers and fewer gastric cancers are seen in countries where the environmental content of those carcinogens is high.

0281 CONTRACEPTIVES AND DYSPLASIA: HIGHER RATE FOR PILL CHOOSERS. (E.) Stern, E. (Sch. Publ. Hlth., U. California, Los Angeles), V. A. Clark and C. F. Coffelt. *Science* 169(3944):497-498, 1970.

Women enrolling in a family planning program were surveyed to determine if there was any relation between use of the oral contraceptive and incidence of cervical cancer. Of 166 women found to have cervical dysplasia prior to selection of a contraceptive method, 122 or 75% chose birth control pills, while 1354 out of 2220 women without dysplasia (61%) chose other methods. The women choosing the pill differed from those choosing IUD's in having a higher income and lower body wt, but no further differences were found over a wide range of demographic and biomedical characteristics, including religion, ethnic group, age, age at first intercourse, age at first pregnancy and number of children.

0282 CERVICAL CYTOLOGY AND MYCOPLASMA IN TWO POPULATIONS. (E.) Gregory, J. E. (Temple U. Sch. Med., Philadelphia, Pa.) and F. E. Payne. *Acta Cytol* 14(7):434-438, 1970.

The possibility of a correlation between mycoplasma infection and carcinoma was investigated in a study of cervical cytology in 2 groups of 150 women. One population was composed of patients visiting a venereal disease clinic; women attending a family planning clinic constituted the other group. The women were of similar socio-economic background, and ages ranged from 16 to 61 yr in the Venereal Disease (VD) group and from 15 to 45 in the Family Planning (FP) population. The prevalence of mycoplasma in the cervix of VD women was 92%, nearly 3 times as high as that in the FP subjects. *Mycoplasma hominis* Type 1 was the predominant species of mycoplasma that was recovered from both groups. Neither age nor the menstrual cycle significantly influenced the prevalence of mycoplasma in either population. In the FP women, observable cellular abnormalities occurred somewhat more often in women using oral hormones than in those using the intrauterine device or not employing any form of contraception. The proportion of abnormal smears was higher in the FP women than in the VD females, but mycoplasma did not significantly influence the occurrence of cellular abnormalities in either population. It is doubtful that a causal relationship exists between contraceptive technique and mycoplasma in the cervix.

0283 THE INCREASING INCIDENCE OF CENTRAL NERVOUS SYSTEM LEUKEMIA IN CHILDREN. (E.)

Evans, A. E. (Child. Hosp., Philadelphia, Pa.), E. S. Gilbert and R. Zanstra. *Cancer* 26(2):404-409, 1970.

Factors which may influence the incidence of CNS leukemia infiltration were investigated in a study of 209 children with acute leukemia, all of whom received the same chemotherapeutic agents. The incidence of symptomatic CNS leukemia was 51% (106/209), 97/173 of whom had lymphocytic or undifferentiated leukemia and 9/36 had other forms. The median survival was 21 months for patients with acute lymphocytic leukemia and 9 months for the other cell types. Life-table analysis showed a median survival of 8 months for patients who had developed CNS leukemia and 24 months for those free of the complication. Age, sex, hematologic status, and chemotherapy regimen did not influence the incidence. The increasing survival of children with leukemia appears to be the chief cause for the increased incidence of CNS leukemia.

0284 CANCER IN IRAN: A STATISTICAL STUDY. (Fr.)

Habibi, A. (Fac. Med. Teheran, Iran). *Bull Cancer* 57(1):133-150, 1970.

In order to obtain information on the prevalence of various forms of cancer in Iran, 28,069 identified cancer cases from the Teheran vicinity from all social classes and ages were studied. Malignant skin tumors were the commonest form of cancer (21.7%) and appeared to be related to exposure to the sun's rays, skin contact with dirty clothing, and to neglect of personal hygiene. Men were most frequently affected, with the male-female ratio approaching 2:1. Among women, cancer of the cervix was the most common, accounting for 21% of the female cases and, like skin cancer, occurred most frequently in patients of the lower social classes. Cancer of the lymphatic glands was widespread (8.1% of all cancer cases); it predominated in men, but occurs in all age groups. Breast cancer occurred in 6.2% of total cases and was most common among women of higher economic status. Cancer of the esophagus occupied fifth place in the general statistics, constituting 4.2% of the cases. Respiratory tract cancer accounted for 6.1% of total cases, with malignant tumors of the larynx and of the bronchii and lung contributing 3.3% and 2.8% of the total cases, resp.

0285 SALIVARY GLAND TUMORS IN EASTERN GERMANY FROM 1955 THROUGH 1958. (Ger.)

Otto, H. D. (Ear-Nose-Throat Clin., Humboldt U., Berlin, Germany), F. Bockmuhl and H. J. Herold. *Deutsch Gesundh* 25(29):1364-1368, 1970.

Six hundred and eighty-two patients with salivary gland tumors (604 parotid gland tumors and 78 submandibular tumors) were recorded in Eastern Germany between 1955 and 1958. Histological examination revealed 320 malignant tumors of which 265 were located in the parotid gland (120 male and 145 female patients), while 55 were located in the submandibular region (32 males, 23 females). Of 362 polymorphic ade-

nomas, 339 were located in the parotid (120 male and 219 female patients) and 23 were submandibular tumors (5 male and 18 female patients). Malignancy occurred mainly between the age of 60 and 80 and was rare before the age of 40, while polymorphic adenomas occurred at any age. Metastases appeared in 66 (22.6%) of the patients with malignant tumors and were more frequent in submandibular tumors (29%) than in parotid tumors (18.7%). Detailed histological differentiation, diagnosis, clinical symptoms and treatment, as well as literature data are given.

0286 THE EPIDEMIOLOGY OF LUNG CANCER: RECENT TRENDS. (E.)

Wynder, E. L. (Sloan-Kettering Inst. Cancer Res., New York, N.Y.), K. Mabuchi and E. J. Beattie, Jr. *JAMA* 213(13):2221-2228, 1970.

To test the hypothesis that tar is the principal lung cancer inducing factor in cigarette smoking, 340 patients with histologically proven lung cancer of Kreyberg group 1 or group 2 type were interviewed about their smoking habits. The investigation confirmed the close association between cigarette smoking and lung cancer, especially of the squamous and oat cell types. In addition, there was a decreased relative risk for those patients developing lung cancer 10 yr after switching to filter cigarettes, possible due to the lower tar content in filter cigarettes. The risk also declines after complete cessation of cigarette smoking, and appears to approach the risk level incurred by non-smokers after 13 years of abstinence from cigarettes.

0287 CARCINOMA OF THE BREAST IN WOMEN LESS THAN THIRTY YEARS OLD. (E.)

Norris, H. J. (Armed Forces Inst. Path., Washington, D. C.) and H. B. Taylor. *Cancer* 26(4):953-959, 1970.

Survival data on carcinoma of the breast for 135 women less than 30-yr-old were evaluated, and clinical and histologic features of the tumors in this series were examined to determine which features were associated with a particular clinical course; mammary cancer in women under 30 appeared to have a poorer prognosis than in older women. The poor prognosis may be explained by the finding that about 10% of the patients were pregnant or lactating—conditions associated with a higher incidence of axillary lymph node metastasis and lethal outcome. Furthermore, incidence of axillary metastasis was slightly higher in younger women, regardless of pregnancy, and carcinoma frequently (17%) developed in the opposite breast. Finally, patients with 1 or 2 positive axillary lymph nodes did poorer than expected. Despite the overall unfavorable outlook, crude survival was improved by the relative infrequency of deaths from causes other than cancer, as contrasted with that of older women. Also, the prognosis for women under 30 was improved by the relatively high proportion (24%) of low-grade infrequently metastasizing tumors, such as medullary intraductal, juvenile, papillary, and well-differentiated carcinomas. When only infiltrating duct carcinoma was considered, 5-yr survival in young women was 50% at 5 yr and 37% at 10 yr. The 5-yr survival rate for patients without axillary metastasis was 81% and the 10-yr figure was 74%, indicating that patients without axillary metastasis did as well as older women with breast cancer.

0288 HEXOKINASE, DIFFERENTIATION AND GROWTH
 RATES OF TRANSPLANTED RAT TUMORS. (E.)
Know, W. E. (Harvard Med. Sch., Boston, Mass.), S. C.
Jamdar and P. A. Davis. *Cancer Res* 30(8):2240-2244,
1970.

Hexokinase activity was measured in fetal, adult, and regenerating livers of rats, and in 18 different types of transplanted hepatic and nonhepatic rat tumors; findings were compared with measured growth rates in the same tissues and tumors to determine whether there was a correlation between hexokinase activity and growth rate. Concentrations of hexokinase in the transplanted tumors were significantly correlated with measured growth rates, and paralleled the progressive loss of histological differentiation of these tumors. The correlations found confirm the similar relationship already found among hepatomas and extends it to some nonhepatic tumors of the rat. The normal tissues, fetal and regenerating liver, grew equally as fast as the fastest tumors but contained significantly less hexokinase. Glutaminase concentration was also correlated with growth rate, although less strongly than hexokinase concentration.

0289 POPULATION KINETICS OF NORMAL, TRANSFORMING AND NEOPLASTIC CELL LINES. (E.)
Norby, K. (Dept. Path., U. Goteborg, Sweden). *Acta Path Microbiol Scand* 78(suppl. 214):1-29, 1970.

Population kinetics of normal, SV40-transformed, and neoplastic cell lines were studied quantitatively *in vitro* by cinemicrographically determining the effective birth, death, and growth rates during exponential growth, and the cell death probability was determined using both the exponential birth-death equation and a mathematical model of Jagers. Observations relating to various properties of normal and SV40-transformed cells revealed that the inoculum size was inversely proportional to the exponential growth rate, that transformed and neoplastic lines had higher cell densities than corresponding normal lines, that normal lines exhibited a much longer lag phase before mitosis resumed than the transformed species, and that mitotic activity during the observation period was greater for transformed cells than for normal cells. Biochemical analysis indicated unbalanced growth with regard to cytochrome oxidase (decrease with time) and ³H-leucine incorporation (increase with time), but balanced growth with regard to lactic dehydrogenase. In fetal human lines, the SV40-transformed lines showed higher mean mitotic times (27.20-34.05 min) than normal lines (24.34-28.47 min); the normal juvenile line BP211-2 had a longer mean mitotic time (37.75 min) than the normal fetal lines but shorter than the juvenile neoplastic line (39.00 min). The mean mitotic times for the Syrian hamster neoplastic lines were considerably longer (28.81-32.29 min) than the normal hamster lines (18.24-18.65 min). The normal cell lines exhibited a high death rate compared with the birth rates, while the SV40-transformed lines, the human neoplastic line and the hamster neoplastic lines had low death rates. Transformed cells and the neoplastic lines often have a lower birth rate than the normal lines, but a higher growth rate and a low death probability

(3.5-18.2% for normal fetal lines and 0 to 0.2% for transformed lines). Reduced cell death and prolonged average life span are characteristic neoplastic changes *in vitro*.

0290 PATTERNS OF GRANULOCYTE KINETICS IN ACUTE MYELOGENOUS AND MYELOMONOCYTIC LEUKEMIA. (E.) Galbraith, P. R. (Dept. Med., Queen's U. Kingston, Ontario, Canada), G. Chikkappa and H. T. Abu-Zahra. *Blood* 36(3):371-384, 1970.

Granulocytes from peripheral blood samples from 25 patients with acute myelogenous leukemia or acute myelomonocytic leukemia were subjected to kinetic studies using radioactive diisopropylfluorophosphate to investigate the more differentiated cells present. Leukocytes were labeled *in vitro* and then returned into the circulatory system. The patterns of disappearance of *in vitro* labeled leukocytes from the blood, and the patterns of emergence of *in vivo* labeled leukocytes from the bone marrow were variable. Nonuniformity in the results suggests that the terms acute myelogenous leukemia and acute myelomonocytic leukemia cover a spectrum of disorders, and that broad generalizations concerning their kinetics cannot be made. The variation in the data suggests that the mature neutrophils in the blood of leukemic patients may arise from abnormal or leukemic precursors.

0291 THE GROWTH CHARACTERISTICS OF AN ASCITIC PLASMACYTOMA (MP 5563) TERMINATING BY FISTULOUS COMMUNICATION WITH THE BLOOD STREAM. (E.) Fakhri, O. (Roy. Postgrad. Med. Sch., London, England). *Brit J Cancer* 24(2):389-394, 1970.

Cells from an ascitic plasmacytoma were injected i.p. into mice (0.2 ml of fluid containing 5 million tumor cells/ml), and the growth of the plasmacytoma was monitored by ⁵¹Cr-RBC dilutions within the peritoneal cavity together with differential cell counts and protein measurements. Following the i.p. transplantation, there was a latency period of 4 days, possibly explained as only a 5% survival of the inoculum. This was followed by logarithmic growth from 4 to 8 days with a doubling time of 18 hr, always similar in different animals. Eventually, after 8 days and after about 100 million cells, an asymptote was reached which was apparently due to a fistula-like communication between blood-stream and peritoneal cavity. This terminal phase (9-10 days) was rapidly followed by death of the mouse.

0292 NATURAL CAUSES OF VARIATIONS IN THE WEIGHT OF SARCOMA 180. (E.) Austin, J. P. (Unilever Res., Welwyn Garden City, Hertfordshire, England) and E. M. Glaser. *Brit J Cancer* 24(2):398-406, 1970.

Male and female mice of differing strains were implanted in the axillary regions with sarcoma 180 tumors and then maintained in environments varying in temperature, in order to test the effects of temperature, sex and strain on the weights attained by the implanted sarcomas. In 2 strains of mice (Swiss and hybrid) in which both sexes were studied the

tumor weights were lower in females; in 3 varieties the tumors weighed less at lower environmental temperatures than at higher ones. At 3 environmental temperatures in the physiological range (7, 24, and 35.5°C) the surfaces were cooler than the adjacent skin, and the tissues of tumors were cooler than the surrounding subcutaneous tissues. These differences were greater in cooler than in warmer environments and increased as tumors grew larger. There were no histological changes to account for the different tumor weights at different environmental temperatures, and it seems probable that tumors are unable to maintain their temperature and their metabolism in cool environments. Mice of the same breed maintained at room temperature showed a pattern of tumor development in which the largest tumors developed in the smallest mice.

- 0293 BEHAVIOR OF MINIMUM-DEVIATION HEPATOMAS IMPLANTED INTO CHICK EMBRYO BLASTODERMS. (E.) Sherbet, G. V. (Inst. Cancer Res., London, England). M. S. Lakshmi and H. P. Morris. *J Nat Cancer Inst* 45(3):419-428, 1970.

Six Morris hepatomas differing in growth rate and karyotype deviation were implanted into 16-18 hr chick embryo blastoderms, and their behavior and specificity of interaction with the embryo cells were assessed. Grafts placed between the embryonic germ layers showed considerable mobility ("takes") and the frequency of "takes" was related to their growth rate. Normal heterografts were invariably covered on all sides by large masses of host mesoderm, except on the side opposed to the endodermal layer of the embryo; the response elicited by Morris hepatomas did not differ significantly from that of normal liver. The hepatomas also induced a characteristic proliferation of the embryonic endodermal cells, but 4 types of tumor cells of mesodermal origin did not have this ability. The extent of both host mesodermal and embryonic endodermal responses appeared to depend on the degree of karyotype deviation. The responses were diametrically opposite but complementary and constant, whether the grafts were derived from hepatomas or from normal liver. These parameters of behavior may be used to assess the degree of tumor progression, differentiation and to detect early neoplastic changes or tendencies in normal tissues.

- 0294 DATA ON THE MORBIDITY AND THE ETIOLOGY OF MAMMARY CANCER IN MAN. (Hum.) Malak, G. (Dept. Surgery, Natl. Inst. Oncology, Budapest, Hungary). *Magyar Onkol* 14(2):84-92, 1970.

- 0295 ON THE REDUCTION OF CANCER MORTALITY: GRAHAM CRAWFORD'S EXPERIMENT, 1949-1969. (E.) Garrett, W. J. (Roy. Hosp. Women, Sydney, Australia). *Med J Aust* 57(25):1239-1243, 1970.

- 0296 CANCER DEATH RATES BY CITE AND SEX FOR RELIGIOUS AND SOCIOECONOMIC GROUPS IN NEW YORK CITY. (E.) Seidman, H. (American Cancer Soc., New York, N. Y.). *Environ Res* 3(3):234-250, 1970.

- 0297 CERVIX CANCER DEATH RATES AND MASS CYTOLOGIC SCREENING. (E.) Christopherson, W. M. (U. Louisville Sch. Med., Kentucky), J. E. Parker, W. M. Mendez and F. E. Lundin, Jr. *Cancer* 26(4):808-811, 1970.

- 0298 FEMALE CANCER IN QUEBEC. (Fr.) Audet-Lapointe, P. (Fac. Med. U. Montreal, Quebec, Canada). *Un Med Canada* 99(8):1464-1469, 1970.

- 0299 BILATERAL OR UTERUS ASSOCIATED CARCINOMA OF THE BREAST. (It.) Garusi, G. (Major Civ. Hosp. Verona, Italy) and E. Donati. *Tumori* 56(2):83-91, 1970.

- 0300 RELATION OF DURATION OF EMPLOYMENT AND PRIOR RESPIRATORY ILLNESS TO RESPIRATORY CANCER AMONG BERYLLIUM WORKERS. (E.) Mancuso, T. F. (Dept. Occup. Hlth., U. Pittsburgh, Pa.). *Environ Res* 3(3):251-275, 1970.

- 0301 PRIMARY PULMONARY MUCOEPIDERMOID TUMORS IN THE GOAT. (E.) Altman, N. H. (Johns Hopkins Med. Sch., Baltimore, Md.), C. S. Streett, R. E. Whitmire, Jr., J. Y. Turner and R. Squire. *Cancer* 26(3):726-732, 1970.

- 0302 AUTORADIOGRAPHIC ANALYSIS OF THE CELL CYCLE OF FIVE SOLID HUMAN TUMORS *IN VITRO*. (E.) Kucheria, K. (Inst. Child Hlth., London, England). *Brit J Cancer* 24(2):283-289, 1970.

- 0303 GROWTH BEHAVIOUR OF HUMAN BRAIN TUMORS IN MATRIX CULTURES IN FRESH AUTOLOGOUS SERUM. (E.) Holmstrom, T. (3rd Dept. Path. U. Helsinki, Finland), E. Saksela, S. Nystrom and E. Saxen. *Acta Path Microbiol Scand* 78(3):313-322, 1970.

- * Rev (0006) (0013) (0018)
- * Chem (0060) (0109) (0117) (0118) (0121)
- * Path (0260)

0304 ENVIRONMENTAL INFLUENCE ON EXPERIMENTAL TERATOCARCINOGENESIS IN TESTES OF MICE.

(E.) Stevens, L. C. (Jackson Lab., Bar Harbor, Me.). *J Exp Zool* 174(4):407-414, 1970.

The importance of hormone concentration and temperature in experimental teratocarcinogenesis was determined by following the grafts of male genital ridges from 12- or 13-day fetuses to various sites in adult mice of strains 129, A/He, and their F₁ hybrids. In grafts to scrotal sites (epididymis, epididymal fat pad, and testis) in the 129 strain, the incidence of teratomas was 61%, 44%, and 82%, resp., compared to the spontaneous incidence of 10%. In the A/He strain 12-day grafts resulted in 60%, 47%, and 43% incidence rates, resp., while in the hybrids the incidence was 61%, 51%, and 90%. Grafting of genital ridges to extra-scrotal sites (spleen, liver, kidney, renal fat pad, and ovarian fat pad) resulted in an overall incidence of 8% in the 129 strain and no teratomas in the A/He strain indicating that these sites do not favor teratocarcinogenesis; however, an overall occurrence of 3% in the hybrid strain was much higher than the spontaneous incidence, indicating that some factor involved in these grafts was teratocarcinogenic. Grafting to unilaterally cryptorchid hosts demonstrated the role of the lower temperature in the descended testes with 5% incidence in strain 129 with descended testes compared to 45% in cryptorchid testes, and 42% and 4%, resp., in the A/He strain. The incidence of teratomas was not significantly different in hosts receiving testosterone (70 µg daily beginning 2 weeks before grafting) from that in non-injected hosts (7% and 3%, resp.) so that sex hormones are not implicated in the experimental production of teratomas.

0305 THE RATIO OF ALBUMIN SYNTHESIS TO TOTAL PROTEIN SYNTHESIS IN NORMAL RAT LIVER, IN HOST LIVER, AND IN MORRIS HEPATOMA 9121. (E.)

Rotermund, H. M. (Biochem. Inst. U. Freiburg, Germany), G. Schreiber, H. Maeno, U. Weinssen and K. Weigand. *Cancer Res* 30(8):2139-2146, 1970.

The ratio of albumin synthesis to total protein synthesis was studied in livers from normal rats and rats bearing Morris hepatoma 9121 injected with radioactive leucine 12 min prior to sacrifice. Within this time, no newly synthesized radioactive protein had left the liver, since labeled protein appeared in the blood no earlier than 15 min after injection. Albumin was purified from livers and hepatomas to constant specific radioactivity. The specific radioactivity of albumin purified from normal liver was 100 times higher than that of albumin from tumor. In normal liver, the radioactivity incorporated into albumin was 3.7% of that found in total protein, and in host liver, 2.8% of total protein radioactivity was found in albumin; in hepatoma only 0.36% of labeled leucine incorporated into protein was measured in albumin. Albumin synthesis appears to be greatly decreased in Morris hepatoma 9121 compared to normal liver.

0306 STUDIES ON THE MECHANISMS OF INVASION IN CANCER: I. ISOLATION AND PURIFICATION OF A FACTOR CHEMOTACTIC FOR CANCER CELLS. (E.)

Yoshida, K. (Kumamoto U. Med. Sch., Japan), T. Ozaki, K. Ushijima and H. Hayashi. *Int J Cancer* 6(1):123-132, 1970.

The pseudoglobulin fraction of certain animal and human tumor tissues (gastric cancer, hepatoma, and a renal metastasis of myeloid leukemia) yielded a protein substance (molecular wt approximately 70,000) chemotactic for cancer cells. It was highly purified by column chromatography using Sephadex G-50 and CM-Sephadex and then by disc electrophoresis; it behaved as a homogenous substance on disc electrophoresis. The substance was thermolabile and had no proteolytic activity. The material was similarly active for rat ascites hepatoma AH109A cells, mouse ascites hepatoma MH134 cells and mouse myeloid leukemia C-1498 cells, suggesting a common chemotactic action. It was ineffective for polymorphonuclear leukocytes of rats. The protein fraction from normal skin and muscle showed no such chemotactic efficacy.

0307 COMPARISON OF ERYTHROPOIETIN RESPONSE IN MICE FOLLOWING POLYCYTHEMIA INDUCED BY TRANSFUSION OR HYPOXIA. (E.)

OKunewick, J. P. (Allegheny Gen. Hosp., Pittsburgh, Pa.) and D. Fulton. *Blood* 36(2):239-245, 1970.

Male mice were given s.c. injections of erythropoietin (6 U/25g body wt) to assess the response to erythropoietin during the first 2 wk after the induction of polycythemia by hypoxia or by transfusion. A 50% higher level of iron incorporation was observed with hypoxia-induced polycythemia compared to transfusion-induced polycythemia. An alteration in both the compartment size and the cell cycle time of the erythropoietic stem cell in mice exposed to prolonged hypoxia may account for this difference.

0308 A STUDY OF ENVIRONMENTAL INFLUENCE UPON SALIVARY GLAND NEOPLASIA IN RATS. (E.)

Rowe, N. H. (Sch. Med., U. Michigan, Ann Arbor), F. C. Grammer, F. R. Watson and N. H. Nickerson. *Cancer* 26(2):436-444, 1970.

Weanling rats (230) were randomized into 7 groups and subjected to conditions of vitamin A deficiency, hypercortisonism, hyperthyroidism, a combination of the last 2, and a windy, cold and humid environment to test the effects of these conditions on submaxillary salivary glands challenged with implanted 7,12-dimethylbenzanthracene; the aim was to develop an animal model for the relationships between nutritional, endocrine and thermal carcinogenic co-factors and the high incidence of salivary gland cancer in Arctic Eskimos. Animals were sacrificed at 14 weeks. Of the 7 regimens, only vitamin A deficiency increased malignant epithelial neoplasm yield (56% compared to 19% in control animals). The other 6 groups showed no significant differences.

0309 CYTOPLASMIC RIBONUCLEIC ACID SYNTHESIS IN THE PREREPLICATIVE PHASE OF ISOPROTERENOL-INDUCED CELL PROLIFERATION. (E.)

Baserga, R. (Temple U. Sch. Med., Philadelphia, Pa.) and T. Sasaki. *Exp Molec Path* 13(1):25-35, 1970.

MISCELLANEOUS

The appearance of radioactivity in the cytoplasmic RNA of pooled salivary gland homogenates prepared from mice injected with ^3H -uridine following i.p. administration of isoproterenol (0.8 $\mu\text{moles/g}$ body wt), a compound known to induce DNA synthesis and cell proliferation, was studied. The minimum time required for the appearance of radioactivity in cytoplasmic ribosomal RNA was the same in unstimulated and stimulated glands; however, the incorporation of ^3H -uridine into cytoplasmic rRNA was much higher in stimulated than in control glands, at 8, 18 and 20 hr after isoproterenol administration. The increase in incorporation of ^3H -uridine was essentially the same in free and membrane-bound ribosomes, and this increase was completely inhibited by inhibitors of isoproterenol-stimulated DNA synthesis such as actinomycin D and cycloheximide. The incorporation of ^3H -uridine into polydisperse (6 S-16 S) cytoplasmic RNA increased sharply at 8 hr after isoproterenol. Evidently, gene activation becomes notable only several hr after administration of isoproterenol in mouse salivary glands.

- 0310 ISOLATION OF MYCOPLASMA FROM LEUKEMIC AND NONLEUKEMIC PATIENTS. (E.) Murphy, W. H. (U. Michigan Med. Sch., Ann Arbor), C. Bullis, L. Dabich, R. Heyn and C. J. D. Zarafonitis. *J Nat Cancer Inst* 45(2):243-251, 1970.

Various methods for isolating *Mycoplasma* spp (mycoplasma) from clinical specimens obtained from leukemic and nonleukemic patients were examined for a relative effectiveness. From 1,950 specimens, 71 strains of mycoplasma were isolated, twenty-seven of which were isolated directly on artificial media. Various basal media, with and without additives, were tested for their capacity to grow mycoplasma from clinical specimens. None of the commonly used media containing fresh yeast extract were clearly superior or inferior to others. Cell culture methods were about 4-fold more effective than direct bacteriologic methods. The combined use of fresh specimens, direct bacteriologic, and cell culture methods for isolating mycoplasma gave an overall frequency of recovery of about 3%. In general, bone marrow specimens were positive less frequently than peripheral blood specimens. Mycoplasma were isolated more frequently from children than from adults, and specimens from leukemic children at diagnosis, or when disease was in relapse, were positive most frequently; specimens from children with nonlymphoid malignancies or blood dyscrasias, also were positive frequently. The evidence from this study suggests that mycoplasma, normally inhabiting the mucous membranes, enter the bloodstream and either persist or multiply in patients with leukemia, lymphoma, or other diseases which depress immunity, but are not significant as a prime etiologic agent.

- 0311 FOCAL AVILLOUS HYPERPLASIA OF THE MOUSE DUODENUM. (E.) Seronde, J., Jr. (Harriet G. Bird Mem. Lab., Stow, Mass.). *J Path* 100(4):254-248, 1970.

A synthetic diet deficient in pantothenic acid was given to mice in order to produce hyperplastic avillous mucosa in their proximal duodenum, which were

examined by light microscopy. The lesions were flat plaques composed of large numbers of parallel tubules derived from the crypts of Lieberkühn. The glandular epithelium was anaplastic at deeper levels, and 2 or more tubules tended to combine to form common passage near the surface. The lesions were small and rare in mice fed on a stock diet, conspicuous in mice fed on a complete synthetic diet, and more severe when pantothenic acid was omitted from the synthetic diet. The lesions probably arise through continuing multiplication of crypt epithelial cells, combined with a failure of their differentiation into mature villus cells. Acute superficial necrosis and ulceration occurring on areas of avillous hyperplasia, and sometimes followed by characteristic deep chronic ulceration were encountered in pantothenic acid-deficient mice.

- 0312 EFFECTS OF ERGOCORNINE AND 2-Br- α -ERGOKRYPTIN (CB-154) ON THE FORMATION OF MAMMARY HYPERPLASTIC ALVEOLAR NODULES AND THE PITUITARY PROLACTIN LEVELS IN MICE. (E.) Yanai, R. (Natl. Cancer Ctr. Res. Inst., Tokyo, Japan) and H. Nagasawa. *Experientia* 26(6):649-650, 1970.

The effects of ergocornine and 2-Br- α -ergokryptin on the formation of mammary hyperplastic alveolar nodules and on the pituitary prolactin levels were determined in 7-8-months-old multiparous C3H/He female mice more than 1 month after the last lactation. Mice were treated with s.c. injections of 0.2 mg ergocornine methanesulfonate or 2-Br- α -ergokryptin daily for 20-23 days and sacrificed when they showed proestrous to estrous smears. The number of hyperplastic alveolar nodules and the degree of lobulo-alveoli formation were decreased 54% and 40% resp., in treated mice compared to controls. The anterior pituitary weight decreased about 20% and the prolactin content fell approximately 45% in treated mice compared to controls. Ergocornine and 2-Br- α -ergokryptin appear to lower pituitary prolactin contents and concentrations, and secondarily inhibit development and growth of hyperplastic alveolar nodules.

- 0313 CYTOPATHOLOGY OF CERVICAL SQUAMOUS CARCINOMA *IN SITU* IN POSTMENOPAUSAL WOMEN. (E.) Tweeddale, D. N. (U. Kentucky Coll. Med., Lexington) *Acta Cytol* 14(7):363-369, 1970.

Two groups of women with cervical squamous carcinoma *in situ*, 1 consisting of women between 24-49 yr old (the premenopausal group), and 1 consisting of women between 50-81 yr old (the postmenopausal group) were studied to investigate the differential cytologic features in the 2 groups. The most important differentiating cytologic features between postmenopausal and premenopausal women is that the former have a greater number of malignant cells with keratinizing tendencies and a lesser number that are parabasal. Also, postmenopausal women commonly have an unusual background resembling necrosis seen with invasive cancer. Postmenopausal women having only *in situ* cancer may be incorrectly diagnosed as cases of invasive malignancy due to a combination of these cytologic findings.

14 ETIOLOGY OF BONE CANCER AND SOME OTHER CANCERS IN THE YOUNG. (E.) Hems, G. (U. d. Buildings, Aberdeen, Scotland). *Brit J Cancer* (2):208-214, 1970.

comparison of growth velocities during adolescence with histograms for bone cancer mortality in England and Wales showed that changes in bone tumor development followed closely the growth changes at adolescence, with a lag of less than 2 or 3 yr between growth peaks and modal ages for bone cancer mortality. Distinct accumulations in the second and third decades of life could also be recognized for cancer of the ovary, testis, prostate and thyroid, suggesting that these accumulations might be associated with rapid growth and development occurring at puberty. The exposure of bone, ovary, testis and prostate to carcinogens might result in a higher incidence of cancer if that exposure occurred before puberty.

15 POLYAMINE SYNTHESIS IN RAPIDLY GROWING TISSUES. (E) Snyder, S. H. (Johns Hopkins Sch. Med., Baltimore, Md.) and D. H. Russell. *J Proc* 29(4):1575-1582, 1970.

Polyamines (associated with rapid tissue growth) are formed by a combination of ornithine and S-adenosylmethionine which have been decarboxylated, possibly by the same enzyme, and the activity of ornithine decarboxylase were determined in regenerating rat liver, in developing chick embryo, and in certain tumors by estimating $^{14}\text{CO}_2$ evolved after incubation with ornithine- $1\text{-}^{14}\text{C}$. As early as 1 hr after partial hepatectomy ornithine decarboxylase activity increased 3-fold (30 mμC/30min/g) in the rat liver; 1 hr after partial hepatectomy the activity had risen to 25 times the control values. In the chick embryo ornithine decarboxylase reached a peak activity (530) at 5 days then gradually declined to no detectable activity at 20 days. Analysis of histidine and ornithine decarboxylase activities in tumors revealed an inverse relation between them. A hepatoma, STAT-3 sarcoma, and NRF-TFF carcinoma had high histidine decarboxylase (35.6, 10, and 22.2, resp.) and low ornithine decarboxylase (11.6, 2.7, and 3.1, resp.) activities, while STAT-1 sarcoma had a high ornithine decarboxylase (11.2) and a low histidine decarboxylase (2.5) activity.

16 NASOPHARYNGEAL CARCINOMA IN CAUCASIAN SIBLINGS: REPORT OF TWO CASES. (E.) R. B. (U. Tennessee Coll. Med., Memphis) and A. Maguda. *J Tennessee Med Ass* 63(9):753-754, 1970.

Case of sibling occurrence of nasopharyngeal carcinoma in Caucasians (a relatively unusual tumor in Caucasians) is described. Geographical contiguity with another reported case of nasopharyngeal carcinoma was noted, but it was not assumed that the contiguity was attributable to more than chance. In neither sibling described was there any history of exposure to chemicals or industrial toxins; neither sibling used alcohol regularly, al-

though one of them commonly smoked one and a half packs of cigarettes daily.

0317 EXTRAUTERINE GROWTH OF MOUSE EGG-CYLINDERS RESULTS IN MALIGNANT TERATOMA. (E.) Solter, D. (Fac. Med. Zagreb, Yugoslavia), N. Skreb and I. Damjanov. *Nature* 227(5257):503-504, 1970.

The effect of mouse egg-cylinders transplanted to extrauterine sites was investigated. Egg cylinders isolated from pregnant uteri of C3H/H mice were transplanted under the kidney capsule of each of 21 3-month-old male mice of the same strain. At sacrifice, an average of 6 months after transplantation, 11 animals had teratomas weighing 0.5-3.5 g, and 10 animals had tumors weighing 7-15 g at 4 months after transplantation. All tumors were sharply demarcated from the kidney parenchyma, and no metastases were found. Histological examination showed that the small tumors were composed predominantly of mature differentiated tissues originating from all three germ layers; in addition, the large tumors were comprised of up to 50% undifferentiated epithelial or mesenchymal tumors.

0318 CHRONIC LYMPHOCYTIC LEUKEMIA AND SUBSEQUENT CANCER IN THE SAME PATIENT. (E.)

Stavraky, K. M. (Dept. Commun. Med., U. Western Ontario, London, Canada), T. A. Watson, D. F. White and E. M. Miles. *Cancer* 26(2):410-414, 1970.

The occurrence of second cancers diagnosed after the onset of chronic lymphocytic leukemia was examined in 258 patients to see if a relationship existed between the leukemia and second cancers. In 825 person-years of observation, 13 second cancers appeared after diagnosis of chronic lymphocytic leukemia, but this occurrence was no greater than that expected in the normal population. No relationship appears to exist between chronic lymphocytic leukemia and other cancers.

0319 THE EFFECT OF HYPERMETHYLATION ON THE FUNCTIONAL PROPERTIES OF TRANSFER RIBONUCLEIC ACID: RIBOSOME-BINDING AND POLYPEPTIDE SYNTHESIS. (E.) Hay, J. (Coll. Physicians Surgeons, Columbia U., New York, N. Y.), D. J. Pillinger and E. Borek. *Biochem J* 119(3):587-593, 1970.

Since tRNA of tumor tissue has an abnormal methylated base content, the action of hypermethylated (dimethylsulfate method of Pillinger, Hay and Borek) tRNA (*Escherichia coli* tRNA) in an *in vitro* ribosome-binding assay and a polypeptide-synthesizing system was studied. The hypermethylated tRNA proved stable under the ribosome-binding assay conditions and was able to bind to ribosomes with the same efficiency as normal tRNA after the proportion of amino acid residues present was adjusted. The relative ability of the hypermethylated tRNA to form polyphenylalanine *in vitro* was inversely proportional to the amount of methylation with an absolute value of 80% inhibition. Polylysine synthesis was 60% inhibited while poly-L-proline was 100% inhibited by 7 mole% hypermethylated tRNA. Aminoacylation (for-

MISCELLANEOUS

mation of the aminoacyl-tRNA) was less affected by hypermethylation, with polylysine synthesis again less sensitive (22% inhibition) than polyphenylalanine (50%) and polyproline (50%) syntheses.

- 0320 MURAMIDASE IN POLYCYTHEMIA VERA. (E.) Binder, R. A. (Mount Sinai Hosp., New York, N. Y.) and H. S. Gilbert. *Blood* 36(2):228-232, 1970.

Serological studies were performed on 45 patients with polycythemia vera in order to confirm the presence of increased muramidase in this condition and to study the relationship of the muramidase level to other features of polycythemia vera. The serum muramidase levels of the polycythemia vera patients were significantly elevated above the values in 20 normal subjects (12-16 $\mu\text{g/ml}$ vs. 9 $\mu\text{g/ml}$). The patients with polycythemia vera who were studied included those with active disease, those controlled with myelosuppressive agents and those in the spent phase. A high degree of correlation was found between muramidase levels and leukocyte count, granulocyte count, serum uric acid, serum vitamin B₁₂ content and unsaturated vitamin B₁₂ binding capacity. No correlation was found between muramidase levels and hematocrit, monocyte count and leukocyte alkaline phosphatase activity. The results appear to support the thesis that serum muramidase originates from granulocytes, and the involvement of the granulocyte in the proliferative process responsible for polycythemia vera may be reflected in the elevated levels of serum muramidase in patients with this condition.

- 0321 CARCINOMA OF THE BREAST: ST. VINCENT'S HOSPITAL SERIES, 1954-1965: THE EFFECTS OF CHILDBEARING ON CARCINOMA OF THE BREAST. (E.) Fleming, J. (St. Vincent's Hosp., Sydney, Australia), B. Sheridan, L. Atkinson and G. Scott, *Med J Aust* 57(25):1252-1256, 1970.

A series of 1,840 patients with breast cancer was studied to determine the effect of previous pregnancy and lactation on the disease, the effect of pregnancy and lactation coincident with the onset of the disease and the effect of pregnancy commencing after treatment of carcinoma of the breast. Approximately 24% of cases of breast cancer occurred in women who had "never lactated," (where the comparison group consisted of women who had produced live children whom they might or might not have fed.) Lactation did not appear to influence the stage of the disease with which the patient first presented; however, it did affect the 5 yr survival rates for patients in differing stages of breast cancer, the rate being 70% for those in the second stage of the disease who had not lactated and 57% for those who had. The survival rate for patients who had had a child was 50%, and 60% for those who had had no children. The incidence of breast cancer commencing in pregnancy was 0.6%; the mean age of these patients was 37 yr, and most had had previous pregnancies. The average age of patients who became pregnant after previous treatment for breast cancer was 35.5 yr, and all but 1 had had previous pregnancies.

- 0322 INITIAL STAGE OF HEMATOGENOUS METASTASIS OF ⁵¹Cr-LABELED TUMOR CELLS. (E.) Suemasu, K. (Nat'l. Cancer Ctr. Hosp., Tokyo, Japan), M. Katagiri, Y. Shimozato, M. Mikuni, and S. Ishikawa. *Gann* 61(1):7-15, 1970.

The relationship between initial organ distribution of hematogenously disseminated tumor cells and subsequent patterns of organ metastasis was investigated in male rats were given i.p. injections of ⁵¹Cr-labeled cells of a transplantable lung carcinoma and Yoshida ascites sarcoma. The relationship between the distribution pattern of ⁵¹Cr-labeled tumor cells immediately after intracardiac injection and patterns of organ metastasis 6-14 days after inoculation of non-labeled tumor cells was examined. The distribution of labeled cells/g of organ at 5 min after injection was 14.7, 5.1, 1.4 and 1.4% for lungs, kidneys, brain and adrenals, resp., with the lung carcinoma cells; the distribution of label was 17.5, 2.9, 1.8, 1.2 and 0.8% for lungs, kidneys, liver, spleen and adrenals, resp., with the Yoshida ascites sarcoma cells. Organs which accumulated less label in the initial period than those mentioned above tended to have rare incidences of metastasis. Measurement of the cells by radioactivity indicated that the stay of the cells in the organs was transient and that the ability of tumor cells to pass through organs differed according to the strain of tumor. Such a difference may also influence the organ selectivity of hematogenous metastasis. As time elapsed, tumor cells in the circulation lost their viability, and cellular debris accumulated in the liver and spleen. The half-life of tumor cells which did not metastasize to any organ was evidently not long.

- 0323 POSTMORTEM OBSERVATIONS ON FISCHER RATS WITH LEUKEMIA AND OTHER DISORDERS. (E.) Davey, F. R. (Child. Cancer Res. Found., Boston, Mass.) and W. C. Moloney. *Lab Invest* 23(3):327-334, 1970.

Because of the high incidence of spontaneous leukemia reported among inbred Fischer rats, the pathological features of this and other disorders were followed until natural death or sacrifice at a terminal stage in 43 male and 43 female animals. The average age at death was 23.9 months (range 11-32 months), and a severe pulmonary infection was detected in all the animals at postmortem; 65.1% of the males had interstitial cell tumors of the testis, and 10.4% of the rats had various subcutaneous tumors. Of the 86 rats, 24.4% had leukemia marked by enlarged spleens (average weight of 9.0 g compared to the control nonleukemic value of 0.9 g) and mottled livers. Infiltration of the spleen, liver, lymph nodes, and lungs was observed in all cases, while the kidney, heart, and gastrointestinal tract were less frequently involved. The bone marrow showed evidence of infiltration in only 3 cases.

- 0324 EPIZOOTIC RETICULUM CELL SARCOMA IN A SEQUESTERED COLONY OF JAPANESE QUAILS. (E.) Nishimura, E. T. (U. Hawaii Sch. Med., Honolulu), E. Ross, G. Leslie, H. Y. Yang and Y. Hokama. *Cancer Res* 30(8):2119-2126, 1970.

the epizootic nature and the pathological features of a spontaneous avian leukosis (reticulum cell sarcoma) observed in a sequestered colony of Auburn strain 571 Japanese quails are presented. The incidence of the spontaneous tumor development was 1.8% (30 out of 47 quail), and the tumors appeared when the quail were between 8 and 22 months of age. Gross pathological examination revealed varied degrees of thymic prominence, enlarged spleens, and frequent tumor infiltration of the bursa of Fabricius, liver, duodenum, caeca, and bone marrow. Electron micrographs demonstrated intranuclear spherical bodies (1200 Å diameter) that had hollow centers surrounded by a concentric and fibrillar double wall and contained a small (200 Å diameter), centrally-positioned electron-dense dot. Although these spherical bodies were not encountered in the liver of a few healthy quails, the significance of the particles remains speculative.

25 CHROMOSOME ABNORMALITIES IN POLYPS AND CARCINOMAS OF THE LARGE BOWEL. (E.) Baker, C. (Mount Vernon Hosp., Northwood, Middlesex, England) and N. B. Atkin. *Proc Roy Soc Med* 63 (suppl.):9-10, 1970.

Chromosome abnormalities in polyps of the large bowel which may have malignant potential are described. In contrast to carcinomas, polyps present minimal changes such as the acquisition of 1 or 2 extra C group chromosomes. Carcinomas show a tendency towards the presence of few B, D and G group chromosomes, but this does not appear to be a feature of premalignant lesions. A malignant cell-line probably does not result from such minimal changes as is seen in polyps, but can result if random secondary chromosome changes also occur. (references)

26 JUVENILE POLYPS OF THE COLON AND THEIR RELATIONSHIP TO ALLERGY. (E.) Alexander, H. (Child. Orthop. Hosp., Med. Ctr., Seattle, Wash.), J. B. Beckwith, A. Morgan and A. H. Bill. *Br J Surg* 120(2):222-225, 1970.

The presence of eosinophils infiltrating juvenile polyps of the colon usually denotes an allergic reaction. The possibility that the polyps are a result of allergy was accordingly studied. Questionnaire responses in 13 cases of juvenile polyps and control cases of hernia showed the following: 11 of 13 patients with polyps (85%) had a personal or family history of allergy, whereas only 5 of 18 (28%) with hernia had a similar history; personal history of allergy was present in 46% of children with polyps, and in 17% of children with hernia; family history of allergy occurred in 77% of those with polyps, and in 17% of patients with hernia. These results are statistically significant, and support the hypothesis that allergy and juvenile polyps may be related. These findings characterize more thoroughly the setting in which such polyps may appear, and lend support to those investigators who believe that juvenile polyps have no malignant potential.

0327 CYTOCHEMICAL STUDIES OF SKELETON NEOPLASMS. (E.) Petrova, A. S. (Acad. Med. Sci. USSR, Moscow) and N. A. Probatova. *Folia Histochem Cytochem* 8(2):135-144, 1970.

Data from cytochemical studies of alkaline and acid phosphatases and the PAS reaction in cells of osteogenic sarcoma, osteoblastoclastoma, Ewing's sarcoma, and reticulosarcoma ossis were examined to investigate the enzyme activities in these tumors. An exceedingly high level of the alkaline phosphatase activity was revealed in the cells of osteogenic sarcoma, a moderate activity level, both of alkaline and of acid phosphatases in the cells of Ewing's tumor, and a weak activity of both the hydrolases investigated in the mononuclear cells of osteoblastoclastoma. The high activity of alkaline phosphatase in the cells of osteogenic sarcoma may be an expression of fibrillogenesis, a specific function of osteoblasts.

0328 BONE MARROW COLONIES: STIMULATION *IN VITRO* BY SUPERNATANT FROM INCUBATED HUMAN BLOOD CELLS. (E.) Chervenick, P. A. (U. Pittsburgh Sch. Med., Pa.) and D. R. Boggs. *Science* 169(3946):691-692, 1970.

Blood from healthy adults was incubated for 10-14 days at 37 C in 6.5% CO₂ to give a supernatant which stimulated the growth of granulocytic and mononuclear cell colonies from mouse and human bone marrow; such a stimulant may function to regulate granulocytic and mononuclear cell growth in normal individuals and in individuals with diseases of the hematopoietic system. The stimulant was resistant to heat and freezing, and could not be dialyzed. Supernatants from sonically disrupted cells and irradiated cells had no colony-stimulating activity by 7 days; the addition of sonically disrupted cells or irradiated cells or plasma to an active supernatant reduced its activity by 40%. Results suggest that the stimulating substance is not stored within the cells, but is produced and released during incubation.

0329 MUCOSUBSTANCES IN NORMAL AND IN NEOPLASTIC MAST CELLS OF THE DOG. (E.) Mariano, M. (Sch. Vetr. Med., U. San Paulo, Brazil). *Acta Histochem* 36(1):14-23, 1970.

Mastocytomas from 9 dogs were subjected to histochemical examination to detect mucosubstances present in neoplastic canine mast cells; both benign and malignant tumors were assayed and compared to normal cells. Although glycogen could not be demonstrated in either normal or neoplastic tissue, neutral, sulfated (heparin), and carboxylic (sialic acid) mucosubstances were found in both normal and neoplastic mast cells. Neoplastic cells also appeared to contain a hyaluronic-acid-like mucosubstance, which was characterized by its alcianophilia at pH 2.5, its metachromasia at pH 5.6 and not below, and by its testicular hyaluronidase and pyocyanine lability.

- 0330 MALIGNANT TUMORS AND CHROMOSOMAL ABERRATIONS. (E.) Schuler, D. (U. Med. Sch. Budapest, Hungary) and M. Dobos. *Acta Paediat Acad Sci Hung* 11(1):3-10, 1970.

Chromosome susceptibility to breakage induced by an alkylating agent, R-52, was studied in peripheral blood cell cultures of patients with malignant tumors, to investigate the correlation of chromosomal aberration with malignancy, and to determine if chromosomal aberrations in malignancy patients is a primary or a secondary phenomenon. The literature of chromosome aberrations in malignancies is reviewed, and the authors' own findings are presented. Chromosome breakages and translocation figures appeared in the cells of patients with Fanconi's anemia, a disease which may predispose to leukemia. Unusually high incidence of chromosome breakage was also found in patients with lymphoreticular tumors, Bloom's syndrome and agammaglobulinemia.

- 0331 ACTIVITIES OF DNA POLYMERASE IN HUMAN UROGENITAL TUMORS. (E.) Shimazaki, J. (Sch. Med., Gunma U., Japan), H. Takahashi, H. Nagai and K. Shida. *Gann* 61(1):47-53, 1970.

DNA polymerase activity was assayed in various human urogenital tumors to investigate the relationship between DNA synthesis and malignant growth. In all tissues examined, the enzyme showed 2- to 10-fold higher activity in the presence of heat-denatured DNA than native DNA as the template. In some tumors which exhibited elevated activity of DNA polymerase, there was a large difference between the activity with native DNA and heat-denatured DNA. In benign prostatic hypertrophy and prostatic carcinoma the level of DNA polymerase activity was relatively low; while in testicular tumors, pelvic kidney tumors, some bladder tumors, and Grawitz tumor DNA polymerase activity was high.

- 0332 BONE MARROW COLONY-STIMULATING FACTOR: RENAL INFLUENCE ON SERUM TITERS. (E.) Foster, R. S., Jr. (U. Vermont Coll. Med., Burlington). *J Surg Oncol* 2(1):1-8, 1970.

The factor in mouse bone marrow cells which stimulates the *in vitro* proliferation of bone marrow cells, resulting in the formation of colonies of granulocytic and mononuclear cells, was titrated in the serum of female mice which had undergone either unilateral or bilateral ureteral ligation, or unilateral or bilateral nephrectomy; the aim was to determine if renal mechanisms capable of influencing the response of the serum colony-stimulating factor exist. The serum titer of the colony-stimulating factor was elevated 18 hr following bilateral ureteral ligation and following either unilateral or bilateral nephrectomy. At 3 and 7 days following unilateral ureteral ligation, there was a moderate elevation of colony-stimulating activity. Renal clearance of the colony-stimulating factor influences the titer of the serum colony-stimulating factor.

- 0333 MULTIPLE MYELOMA WITHOUT PARAPROTEIN. (E.) Szucs, J. (U. Med. Sch. Budapest, Hungary). *Haematologia* 4(1):97-102, 1970.

- 0334 INFRARED-EMISSION OF SKIN TUMORS. (Ger.) Brehm, G. (Clin. Johannes Gutenberg U., Mainz, Germany) and K. E. Seeberger. *Arch Klin Exp Derm* 238(3):217-227, 1970.

- 0335 COMPARATIVE EXAMINATIONS WITH RESPECT TO INTERFERON PRODUCTION OF NORMAL AND LEUKEMIC LEUKOCYTES. (Hun.) Hadhazy, G. (Inst. of Microbiol., Debrecen Medical U., Hungary), L. Vaczi, L. Gergely, F. D. Toth and G. Szabo. *Magyar Onkol* 14(2):67-72, 1970.

- 0336 β -AMINOISOBUTYRIC ACID IN URINE FROM PATIENTS WITH BLADDER TUMORS. (E.) Sjölin, K. E. (Sundby Hosp., Copenhagen, Denmark), K. Nyholm and H. R. Nielsen. *Acta Path Microbiol Scand* 78(3):368, 1970.

- 0337 HISTOCHEMICAL DISTRIBUTION OF SOME HYDROLYTIC ENZYMES IN A CASE OF FAMILIAL POLYPOSIS WITH MALIGNANT CHANGES. (E.) Maggi, V. (Imp. Cancer Res. Fund, London, England) and A. P. Wyatt. *Proc Roy Soc Med* 63(suppl.):34-35, 1970.

- 0338 ENZYME ACTIVITY, ACIDIC NUCLEAR PROTEINS, AND PROGNOSIS IN HUMAN BREAST CANCER. (E.) Smith, J. A. (Imp. Cancer Res. Fund, London, England), R. J. B. King, B. F. Meggitt and L. N. Allen. *Brit Med J* 2(5711):698-701, 1970.

- 0339 MALIGNANT TUMORS ARISING FROM SMALLPOX VACCINE SCARS. (Fr.) Geiser, J. D. (U. Clin. Dermatoven, Lausanne, Switzerland). *Praxis* 59(32):1158-1161, 1970.

- 0340 MALIGNANCY RELATED CHANGES IN PERIPHERAL BLOOD SMEARS. (E.) Johnston, B. (St. Vincent's Hosp. Med. Ctr., New York, N. Y.). *Acta Cytol* 14(7):399-403, 1970.

- 0341 CARCINOMA DEVELOPED ON SITE OF ANO-RECTAL FISTULA. (It.) Rimondi, C. (St. Ursula Polyclin., Bologna, Italy), R. Tonti and B. Teofoli. *Cancro* 22(4):451-459, 1970.

- 0342 STEROIDS AND CELL PROLIFERATION: A STUDY ON NORMAL AND PATHOLOGICAL LYMPHOID CELLS *IN VITRO*. (It.) Tarocco, R. P. (Clin. Med. Gen., U. Turin, Italy), G. Benzio, P. Masera, L. Cisiano and V. Gabutti. *Boll Soc Ital Biol Sper* 46(4):157-159, 1970.

- 0343 LYMPHOPROLIFERATIVE SYNDROME WITH ATYPICAL DYSGLOBULINEMIA AND CHROMOSOMAL ANOMALIES. (Fr.) Vagner-Capodano, A. M. (Fac. Med. Marseilles, France), P. Detolle, B. Daumas, H. Arroyo and L. Aubert. *Nouv Rev Franc Hemat* 10(4):541-551, 1970.

DESCRIPTION OF INDEXES

The SUBJECT INDEX is based on a hierarchial system of classification in which *major index terms* are modified by one or more *key word descriptors*. The *key word descriptors* are listed in decreasing order of importance and describe the content of the abstract or citation. In addition, in this indexing system, some *key word descriptors* will also be used as *major index terms*, thus providing in-depth indexing of each document. An abstract or citation number, in brackets, will be found after the *key word descriptors*. Citations will be identified by an asterisk outside of the brackets.

An illustrative example of this indexing system follows:

LIVER

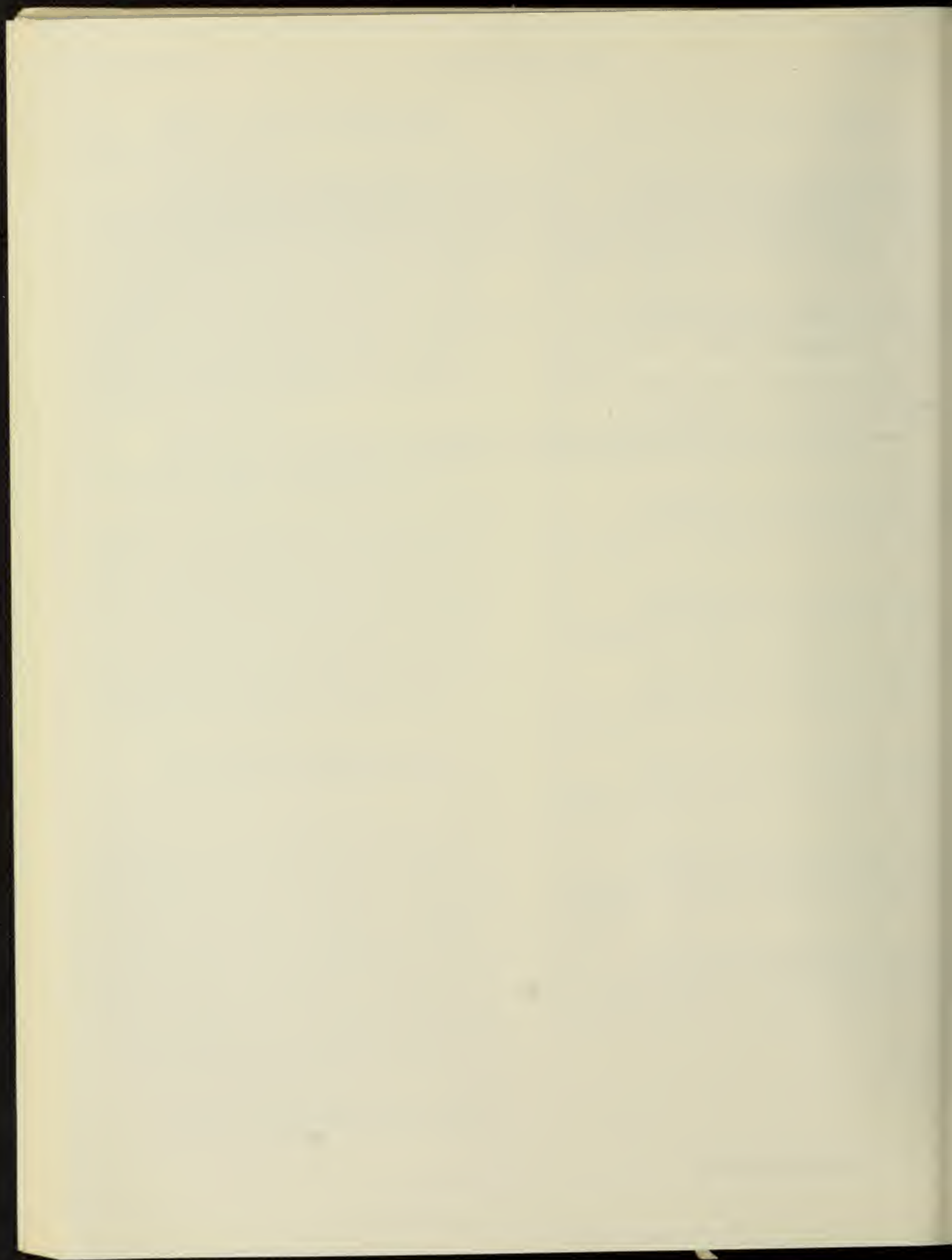
Hepatoma, N,N'-2,7-fluorenylenebisacetamide, X-irradiation

N,N'-2,7-FLUORENYLENEBISACETAMIDE

Hepatoma, X-Irradiation, Accelerated Induction

RADIATION

Hepatoma, N,N'-2,7-fluorenylenebisacetamide, Accelerated Induction



AUTHOR INDEX

AARONSON, S.A.
0199
ARFELSON, H.T.
0167, 0173
ARU-ZAHRA, H.T.
0290
ACKERMAN, A.P.
0134
ADAMSON, R.W.
0073
ADIDINGER, H.V.
0157
ADNET, J.J.
0127, 0128
AISENBERG, A.C.
0155, 0246
ALEXANDER, R.H.
0326
ALEYASSINE, H.
0043
ALEN, I.N.
0330
ALTER, A.A.
0150
ATMAN, M.H.
0301
MRS, F.
0270
METANI, T.
0240
ANDERSON, J.
0182, 0208
ANDERSON, H.G.
0211
ANDERSON, R.F.
0247
ANDRE-SCHWARTZ, J.
0224
ANKERST, J.
0180
ANONYMOUS
0005, 0009, 0010,
0015, 0100, 0113
ANSARI, M.
0235
ARAJ, M.
0126
ARFMAN, F.
0036
ARMSTRONG, W.Y.W.
0224
ARNOLD, W.J.
0164
ARROYO, W.
0342
ATASSI, S.A.
0038
ATKIN, M.D.
0325
ATKINSON, L.
0321
ATREPT, L.
0343
AUDET-LAPOINTE, P.
0298
AUFLIAN, I.
0186
AURORA, A.L.
0274
AUSTIN, J.P.
0292

BADER, A.V.
0204
BADER, J.P.
0204
BAGSHAW, A.
0231
BAKAY, M.
0178
BAKER, M.C.
0225
BAKEFORD, S.
0240
BANKOWICKI, W.A.
0159
BARTLETT, C.
0101
BASEPGA, P.
0300
BASSIN, R.H.
0195
BEATTIE, F.J., JR.
0284
BECKWITH, J.P.
0324
BELADI, J.
0178
BELDOTTI, J.
0224
BELI, C.B.
0316
BENOIT, J.N.
0276
BENZIO, G.
0342
BERGERON, J.L.M.
0256
BERNARD-GRIFFITHS, I.
0242
BETATI, G.
0242
BELL, A.H.
0324
BINDER, P.A.
0320
BISHOP, J.W.
0203
BISTONI, F.
0215
BJERKNES, P.
0074
BLACK, D.A.
0148
BLACKLOW, M.R.
0179
BLAKE, D.F.
0071
BLOTT, F.C.
0274
BLOOM, F.T.
0072
BLUNCK, J.W.
0053
BOCKMUEHL, F.
0285
BOGGS, D.R.
0328
BOLIS, G.R.
0192
BONK, H.
0253

BONNEAU, H.
0241
BOREY, F.
0310
BOUSQUET, W.F.
0071
BRACHMANN, I.
0031
BREHM, G.
0334
BRIEF, P.
0217
BRIEF, W.F.
0160
BROWN, F.V.
0029
BROWN, J.M.
0068
BROWN, M.R.
0206
BRYAN, G.T.
0037, 0038
BULLIS, C.
0310
BURGER, C.I.
0164
BURGOYNE, G.W.
0161
BURKITT, C.P.
0004
BURNBY, A.
0141, 0142
BUSTIN, F.
0240
BUSS, W.
0272
BYKOVSKY, A.P.
0144
CALNEK, R.W.
0157, 0158
CAPUTO, A.
0219
CARRONE, P.P.
0150
CARDEILHAC, P.I.
0048
CARDELLA, T.
0045
CARROLL, W.V.
0062
CASPERSSON, T.
0262
CASTELLI, I.
0219
CATTOOR, J.P.
0187
CAULET, T.
0127, 0128
CEDERLOF, P.
0105
CEMAN, C.
0223
CERVANTES, O.F.R.C.
0125
CHANDRA, S.
0175
CHARNEY, J.
0104
CHAUVERRA, J.
0015

CHEEVERS, W.P.
 0218
 CHERNOZEMSKI, I.M.
 0081
 CHERVENICK, P.A.
 0328
 CHEW, R.K.
 0232
 CHIHARA, G.
 0026
 CHIKKAPPA, C.
 0260
 CHIPIGOS, M.A.
 0171, 0194
 CHOPRA, H.C.
 0144
 CHRISTOPHERSON, W.W.
 0097
 CHU, F.C.W.
 0133
 CHUNG, F.P.
 0073
 CISTANO, I.
 0342
 CITOLIER, P.
 0137
 CLAPP, M.V.
 0080
 CLARK, V.A.
 0281
 CLARKE, G.D.
 0216
 COADY, A.
 0033
 COCHET, G.
 0241
 COFFERT, C.F.
 0281
 COFFEY, C.B.
 0050
 COGGIN, J.H.
 0211
 COHEN, M.W.
 0154
 COHEN, S.W.
 0037, 0030
 COLE, S.P.
 0260
 COLMACHI, M.T.
 0090
 COMBS, G.F.
 0048
 COMMONER, S.
 0042
 CONZELMAN, G.W.
 0027
 COOPER, R.W.
 0073
 COTTALESSO, F.
 0122
 COULET, M.
 0242
 COUTELLE, C.
 0253
 COUTELLE, P.
 0253
 CRAWFORD, M.
 0273
 CRITTENDER, I.R.

0140

DABICH, I.
 0310
 DAFIARY, D.K.
 0247
 DALHAMN, T.
 0107
 DAMJANOV, I.
 0317
 DAS, M.R.
 0141, 0142
 DAUMAS, P.
 0343
 DAVEY, F.R.
 0323
 DAVIS, H.J.
 0186
 DAVIS, J.W.
 0154
 DAVIS, P.A.
 0288
 DEHMEN, W.
 0069
 DELLA PORTA, G.
 0099
 DE MAEYER-GUIGNARD, I.
 0021
 DENMAN, A.W.
 0168
 DENMAN, F.J.
 0168
 DE GCA, W.W.
 0043
 DE GME, K.P.
 0076
 DE PAPP, Z.G.
 0138
 DERINGER, M.K.
 0193
 DETOILE, P.
 0343
 DE VILLIERS, J.M.
 0248
 DIAMANDOROULOS, G.T.
 0209
 DOROS, M.
 0330
 DOMBROWSKI, C.S.
 0124
 DONATI, F.
 0299
 DONNER, I.
 0201
 DORKEN, W.
 0272
 DOSIK, W.
 0150
 DOSTALOVA, C.
 0226
 DOWDIE, W.
 0002
 DRUCKREY, H.
 0022, 0000
 DRESBERG, P.W.
 0202
 DUFF, R.
 0213
 EDDIS, G.T.
 0048
 EILERS, F.P.
 0147

EL ATTAR, C.A.
 0268
 EL-FIKY, S.M.
 0190
 ELY, T.S.
 0115
 ENDERS, J.F.
 0200
 ERB, R.J.
 0075
 ERTURK, F.
 0037, 0038
 EVANS, A.F.
 0283
 EVANS, V.I.
 0063
 EVATT, R.I.
 0264
 FARIANI, A.
 0089
 FAKHRI, O.
 0281
 FALKE, D.
 0188
 FARAGO, L.
 0117
 FASSKE, F.
 0220
 FAUSTO, M.
 0039
 FAVRE, P.
 0241
 FELICETTI, D.
 0253
 FERRERO, A.
 0086
 FETTING, P.
 0220
 FIMIANI, M.
 0215
 FINK, M.A.
 0143
 FISCHINCEK, P.I.
 0195
 FLANDERS, L.F., III
 0027
 FLEMING, I.
 0321
 FLETCHER, C.M.
 0017
 FLEISSBACH, P.
 0272
 FRANCE-ROUSSEAU, M.
 0242
 FONG, C.K.Y.
 0210
 FORSYTH, P.
 0045
 FOSTER, P.S., JR.
 0332
 FOWLER, M.F.
 0033
 FRANKEL, M.W.
 0041
 FRAHMANT, J.F., JR.
 0012
 FRAYSSINET, C.
 0049
 FREL, J.V.
 0088

FRIBERG, I.
 0109
 FRIEDMAN, M.A.
 0046
 FUJINAGA, K.
 0143
 FUKUOKA, F.
 0026
 FULLMER, C.D.
 0104
 FULTON, D.
 0307
 GARUTTI, V.
 0342*
 GAIRRAITH, P.R.
 0290
 GALLAGHER, C.M.
 0047
 GARCIA, H.
 0087
 GARRETT, W.J.
 0295*
 GARNIST, G.
 0299*
 GERHART, F.
 0112
 GEISER, J.D.
 0339*
 GERBER, P.
 0156
 GERGELY, L.
 0335*
 GIBSON, W.T.
 0194
 GILBERT, E.S.
 0283
 GILBERT, W.S.
 0320
 GILFILLAN, R.
 0245
 GILLY, L.
 0135
 GIRARD, M.M.
 0018*
 GIRARD, R.
 0121*
 GLASER, F.W.
 0292
 GLAVIND, J.
 0036
 GLEICHMANN, F.
 0224
 GLEICHMANN, W.
 0224
 GODENECHT, D.
 0242*
 GOETZ, D.
 0152
 GOLD, P.
 0235
 GOLDMAN, J.M.
 0155, 0246
 GOLDSTEIN, A.I.
 0197
 GOLDSTEIN, D.W.
 0274
 GOLDSTEIN, G.
 0156
 GORLICH, M.
 0007

GORLING, R.J.
 0244
 GOTOH, A.
 0151
 GRAPSTAD, H.
 0114
 GRAMMER, F.C.
 0308
 GRANOFF, A.
 0189
 GRANT, G.A.
 0065
 GRANT, R.M.
 0279
 GRANTHAM, P.W.
 0054
 GRAVELL, M.
 0180
 GREEN, M.
 0143
 GREGORY, J.E.
 0282
 GRIMM, J.
 0233
 GROPP, A.
 0137
 GROVER, P.I.
 0067
 GUDNASON, D.
 0013
 GUENET, J.L.
 0128
 GUILLE, F.
 0243*
 GUILLOT, J.
 0242*
 GUINZ, F.W.
 0008
 GURGO, C.
 0143
 HABIBI, A.
 0284
 HADZATY, G.
 0335*
 HAGMAR, R.
 0078
 HAHN, F.C.
 0214
 HAKAMA, M.
 0264
 HAKE, T.
 0226
 HALKETT, J.A.F.
 0225
 HAMAJIMA, K.
 0151
 HANAFUSA, H.
 0204
 HANNA, M.G., JR.
 0174
 HARPER, A.
 0268
 HARRIS, C.
 0024
 HARMWOOD, S.F.
 0211
 HASHIMOTO, Y.
 0055
 HATANAKA, M.
 0204

HATFIELD, P.M.
 0132
 HAUSE, L.I.
 0252
 HAY, J.
 0319
 HAYASHI, H.
 0306
 HEARNE, F.T.
 0115
 HEATH, C.W., JR.
 0266
 HEMPEL, H.C.
 0233
 HEMPELMANN, I.H.
 0138*
 HEMS, G.
 0265, 0314
 HENNEKEFUSER, H.W.
 0137
 HENNINGES, H.
 0074
 HENRY, P.W.
 0209
 HERRER, L.
 0266
 HEROLD, H.I.
 0285
 HEYM, P.
 0310
 HIDAISI, G.
 0178
 HIRAYAMA, T.
 0151
 HIRSCHHORN, K.
 0150
 HIRSBAUM, Y.
 0154
 HOFER, R.
 0019*
 HOGGAN, M.D.
 0179
 HOKAMA, Y.
 0324
 HOLIK, F.
 0229
 HOLLEY, P.W.
 0217
 HOLMSTROM, T.
 0303*
 HODGUE, P.
 0187
 HOFENER, C.
 0128
 HORTO, T.
 0035
 HORN, D.
 0017
 HOSHINO, W.
 0026
 HSU, I.Y.
 0150
 HUI, F.W.
 0154
 HUISERY, R.A.
 0022
 II, Y.
 0267
 IMAI, H.
 0261

IMAT, H.T.
 0102
 IMAMURA, M.
 0092
 IMDGIN, S.W.
 0134
 INOUE, M.
 0153
 INOUE, T.
 0271
 ISAKA, H.
 0097
 ISHIDA, K.
 0267
 ISHIDATE, M.
 0093
 ISHIVAKA, S.
 0322
 ISHIMARU, T.
 0267
 ITO, M.
 0040
 ITO, Y.
 0151
 IVANKOVIC, S.
 0032, 0090
 IVASKOVA, F.
 0227
 IVERSEN, D.H.
 0074
 IVERSON, H.
 0074
 JACKSON, J.
 0203
 JACKSON, S.
 0069
 JACOV, H.W.
 0133
 JAINCHILL, J.L.
 0199
 JAKOBSSON, P.
 0262*
 JAKOBURKOVA, I.
 0227
 JAMPAR, S.C.
 0288
 JANOFF, A.
 0059
 JANSEN, F.
 0270
 JASTY, W.
 0182, 0208
 JEHN, H.W.
 0230
 JENSEN, F.M.
 0175
 JENSEN, M.K.
 0030
 JOHNSON, A.D.
 0133
 JOHNSON, P.W.
 0124
 JOHNSTON, R.
 0340*
 JONES, W.P., JR.
 0254
 JOSEY, W.F.
 0185
 JOSHI, V.V.
 0088

KAFUKO, C.W.
 0004
 KAHL, C.F.
 0180
 KAJI, M.
 0170
 KAPLAN, M.W.
 0246
 KATAGIRI, M.
 0322
 KATCHALSKI, F.
 0236
 KATO, R.
 0093
 KATSUKI, H.
 0094
 KAUFMAN, L.
 0087
 KAWAMURA, A., JR.
 0151
 KAWASHIMA, Y.
 0093
 KEEFER, L.
 0087
 KELLER, J.W.
 0002
 KERR, W.A.
 0043
 KEYDAR, J.
 0141, 0142
 KHODRYARIAN, M.
 0181
 KHOR, H.T.
 0062
 KIMARD, R.
 0003
 KING, R.J.R.
 0338*
 KINGSBURY, D.W.
 0176
 KIPP, W.H.
 0029
 KITTLICK, P.D.
 0084
 KLASSEN, A.
 0059
 KLAMPER, M.R.
 0278
 KLEIN, G.
 0153
 KNIGHT, C.A.
 0148
 KNOW, W.E.
 0288
 KOBAYASHI, H.
 0170
 KOBAYASHI, M.
 0096
 KOHIER, B.F.
 0163
 KOPPEL, W.
 0175
 KOSEK, J.C.
 0131
 KOSHIRA, K.
 0094
 KOSLOWSKI, L.
 0139*
 KRUGER, F.W.
 0082

KURPEY, J.
 0235
 KRUSE, H.
 0032
 KRUSTAK, F.
 0221*
 KUPFLKA, M.
 0229
 KUCHERIA, K.
 0302*
 KUDYKOWSKI, J.
 0262*
 KUADIR, V.
 0103
 KUROKI, T.
 0098
 KYLE, R.A.
 0264
 LAFARGE, C.
 0049
 LAKSHMI, M.S.
 0293
 LAMBERSON, H.V.
 0191
 LAMPER, F.
 0149
 LAMPERT, F.
 0152
 LANDSCHUITZ, C.
 0032
 LANE, D.
 0136
 LAURSEN, R.
 0110
 LAUF, L.R.
 0016
 LAWSON, T.A.
 0028
 LE CLERC, I.C.
 0165
 LEDINKO, N.
 0210
 LEE, K.J.
 0261
 LEE, K.M.
 0163
 LEE, K.T.
 0261
 LEE, K.Y.
 0047
 LEE, S.H.
 0043
 LEE, S.K.
 0261
 LEE, S.L.
 0150
 LEFFALL, L.S.D., JR.
 0273
 LEGGAY, G.
 0127, 0128
 LEGRAND, E.
 0019*
 LEHNERT, G.
 0112
 LENTLE, R.C.
 0111
 LEONG, J.L.
 0070
 LESHER, J.
 0123

ESHER, S.
 0123
 ESLEY, G.
 0124
 EVIN, M.J.
 0209
 EVINE, A.S.
 0209
 EVINSON, W.
 0203
 EVY, J.P.
 0145
 FJINSKY, W.
 0047, 0086, 0087
 GILLY, F.
 0197
 GYSK, J.
 0242*
 GOWNER, A.I.
 0057, 0144, 0145
 GU, C.H.
 0151
 GZTI, F.A.
 0130
 GUIS, C.J.
 0053
 GUITT, J.F.
 0001
 GUE, C.F.
 0185
 GUDLOW, A.
 0214
 GUNDIN, F.F., JR.
 0257*
 GUNDMAN, T.
 0109
 GURICHT, K.
 0284
 GYHALA, D.
 0201
 GACHLEDER, W.
 0014
 GAC MAHON, D.
 0260
 GAENO, H.
 0305
 GAGGI, V.
 0337*
 GAGIDA, T.A.
 0314
 GAJSKY, A.
 0227
 GAJUMBAR, S.K.
 0041
 GAKINO, S.
 0234
 GALAK, G.
 0294*
 GANCINI, I.D.
 0182, 0208
 GANCUSO, T.F.
 0300*
 GANDY, S.H.
 0134
 GANGI, R.J.
 0237
 GARDINEY, M.R., JR.
 0237
 GARIANO, M.
 0329

MARTINADI, H.M.
 0122*
 MARGHARDT, W.
 0258
 MARTIN, G.S.
 0202, 0205
 MARIYAMA, Y.
 0223
 MASERA, P.
 0342*
 MASON, M.V.
 0146
 MASSICOT, J.C.
 0171
 MASUJI, H.
 0098
 MATSUMOTO, M.
 0056
 MATTINGLY, R.F.
 0252
 MATUA, Y.
 0035
 MC BRIDE, R.A.
 0050
 MC CLAMAHAN, M.S.
 0179
 MC DONALD, A.D.
 0248
 MC DONALD, J.C.
 0248
 MC HUGH, P.R.
 0223
 MEADE, H.V.
 0191
 MEDINA, D.
 0076
 MEFE, D.
 0135
 MEGGITT, R.F.
 0338*
 MEHTA, F.S.
 0247
 MEKIER, L.R.
 0207
 MENDEF, W.M.
 0297*
 MESSERSCHMIDT, D.
 0139*
 METZLER, M.
 0031
 MEYER, G.
 0241*
 MICKY, M.D.
 0120*
 MIFTTINEN, D.S.
 0260
 MIKAMI, T.
 0159
 MIKUNI, C.
 0234
 MIKUNI, M.
 0322
 MILES, F.M.
 0318
 MILNE, J.F.H.
 0114
 MIRA, F.
 0251
 MIROFF, G.
 0191

MIRVISH, S.S.
 0083
 MITCHELL, G.W., JR.
 0245
 MKHEIDZE, D.M.
 0057, 0144, 0145
 MOLDNEY, W.C.
 0123
 MONTESANO, R.
 0086
 MORRE, D.H.
 0194
 MORGAN, A.
 0324
 MORIWAKI, Y.
 0102
 MORRIS, H.D.
 0293
 MORTON, D.I.
 0147
 MORTON, J.F.
 0027
 MULLICK, S.
 0245
 MUELVINILL, J.J.
 0012
 MURATA, M.
 0151
 MURPHY, F.
 0125
 MURPHY, F.F.
 0185
 MURPHY, W.H.
 0310
 MUSTACCHI, P.
 0278
 NAGAI, H.
 0331
 NAGASAWA, H.
 0312
 NAGAYO, T.
 0040
 NAHAMIAS, A.
 0002
 NAHMIA, A.J.
 0185
 NAIR, Z.M.
 0185
 NAKAKIKI, Y.
 0172
 NAKAMURA, T.
 0035
 NAMBA, M.
 0094
 NATHANSON, I.
 0230
 NEUMANN, H.C.
 0031
 NEWELL, G.R.
 0260
 NICKERSON, M.H.
 0308
 NIELSEN, W.D.
 0336*
 NIEMCZYK, H.
 0137
 NISHIHARA, F.
 0092
 NISHIHARA, H.
 0092

* indicates a plain citation without accompanying abstract

NISHIKAWA, K.
 0035
 NISHIMURA, F.T.
 0324
 NISHIYAMA, H.
 0267, 0271, 0275
 NORBY, K.
 0289
 NORONHA, F.
 0163, 0164
 NORROTH, K.
 0104
 NORRIS, H.J.
 0287
 NOVELLI, A.
 0122
 NOVODRODINSKY, A.
 0236
 NOYES, W.F.
 0200
 NYHOLM, K.
 0136
 NYSTROM, S.
 0103
 ORARA, Y.
 0234
 ORA, T.
 0094
 ORAKA, T.
 0169
 ODASHIMA, S.
 0055, 0091
 OEHLERT, W.
 0044
 OGARA, R.W.
 0073
 OKUNIEWICK, J.P.
 0107
 OKUMUKI, Y.
 0035
 OLIVI, M.
 0122
 OLSSON, H.
 0109
 OMORI, Y.
 0093
 O'NEAL, R.M.
 0241
 ONGDA, K.
 0093
 ONOFERA, K.
 0212
 OPPENHEIM, S.
 0165
 OSHIRO, K.
 0126
 OTTO, H.D.
 0285
 OYMAN, Y.A.
 0209
 OZAKI, T.
 0104
 PANIJEI, J.
 0238
 PAOLETTI, F.G.
 0089
 PAOLETTI, P.
 0089
 PAPAC, P.J.
 0239

PAPATHEODOROU, T.
 0106
 PARKER, A.M.
 0231
 PARKER, J.F.
 0297
 PARM, L.
 0099
 PASTERNAK, C.A.
 0256
 PATILLO, R.A.
 0252
 PAYNE, F.E.
 0282
 PAYNE, L.N.
 0162
 PEARSON, J.W.
 0196
 PEDLEY, S.F.
 0115
 PELLER, P.
 0152
 PENNEYS, N.S.
 0134
 PERDOMO, J.T.
 0048
 PESTIAU, J.
 0187
 PETROVA, A.S.
 0327
 PHILIP, P.
 0030
 PHILIPS, F.S.
 0058
 PILCH, Y.H.
 0077, 0222
 PILLINGER, D.J.
 0319
 PINCUS, R.A.
 0138
 PINDORF, J.J.
 0247
 PIPER, W.N.
 0071
 PITOT, H.C.
 0051, 0052
 PLATA, F.J.
 0163
 PLISS, G.R.
 0023
 PLIOT, M.
 0127
 POIRIER, L.A.
 0051, 0052
 POLKORNY, J.
 0220
 POOLE, A.R.
 0250
 PRECHTEL, K.
 0152
 PREUSSMAN, P.
 0022
 PRICE, F.M.
 0013
 PRICE, J.M.
 0038
 PROBRATOVA, M.A.
 0327
 PROFFITT, S.D.
 0131

PROPP, S.
 0130
 PRUSKA-KOEPPE, H.
 0257
 PULLINGER, R.D.
 0194
 PURCHASE, H.G.
 0161
 PUSZTAI, R.
 0178
 PYLEVA, Z.A.
 0025
 QUETIER, F.
 0263
 QUINTRELL, M.
 0203
 RABSTEIN, L.S.
 0167, 0173
 RAIKHLIN, M.T.
 0258, 0259
 RAITSCHEN, P.
 0118
 RAMMING, K.D.
 0077, 0222
 RAPP, F.
 0213
 RATH, F.W.
 0253
 RAY, R.K.
 0143
 REDDY, J.
 0024
 REES, F.D.
 0061
 REINER, J.
 0079
 REINHARD, J.F.
 0119
 REIS, H.F.
 0226
 RENNIE, M.
 0162
 RETH, S.
 0220
 REURER, M.D.
 0034
 REVOI, I.
 0121
 RIEDER, S.V.
 0246
 RIMONDI, C.
 0341
 ROBRINS, J.
 0255
 ROE, F.J.C.
 0065
 ROIZMAN, R.
 0002
 ROKUTANDA, H.
 0143
 ROKUTANDA, M.
 0143
 ROSS, F.
 0324
 ROTERMUND, H.W.
 0305
 ROUSE, W.
 0194
 ROWE, H.W.
 0308

YSTON, T.
0186
CKEP, U.
0082
SEELL, D.H.
0315
GERMAN, R.H.
0124
ITO, H.
0170
KSFLA, F.
0303
LAEF, G.B.
0255
LIMI, P.
0254
MAGGIO, J.
0103
MUELS, L.T.
0022
NCEB, A., JR.
0252
NDER, S.
0044
NPE, T.
0151
NTI, I.
0122
SAKI, T.
0309
TO, H.
0098
UER, G.
0214
VEL, H.
0045
XEN, F.
0303
HAFFER, W.
0045
HAGEN, R.
0090
HIEFER, D.
0089
HLESINGER, R.W.
0184
HLOM, J.
0141, 0142
HNEIDER, R.
0277
HOENTAL, P.
0033
HON, F.
0229
HOTTEFFEL, D.
0011
HREJPER, G.
0305
HROEDER, F.C.
0048
HULLER, D.
0330
HULL, M.D.
0132
HMANITZ, G.
0112
HWARD, P.S.
0224, 0230
OTT, G.
0321

SEARLE, J.H.A.
0269
SEERBERGER, K.F.
0334
SEIDMAN, H.
0296
SELIRIO, E.S.
0150
SENDO, F.
0170
SENIK, A.
0165
SENTURIA, R.H., JR.
0042
SENYSYN, J.J.
0133
SERONDE, J., JR.
0311
SEYDEWITZ, V.
0139
SHEININ, R.
0212, 0218
SHERRET, G.V.
0293
SHERIDAN, P.
0321
SHEVLIAGHYN, V.I.
0207
SHIDA, K.
0331
SHIMAZAKI, J.
0331
SHIMOSATO, Y.
0322
SHLYANKEVICH, M.A.
0207
SHORTTRIDGE, K.F.
0183
SHURIN, A.S.
0259
SHUCK, A.
0061
SIBAL, L.R.
0163
SILVERBERG, F.
0272
SILVERSTONE, H.
0240
SIMPSON, W.L.
0060
SIMS, P.
0066, 0067
SINCLAIR, W.K.
0129
SJOGREN, H.O.
0180
SJOLIN, K.F.
0336
SKINNER, M.
0230
SKRER, N.
0317
SLABBER, C.F.
0242
SMITH, J.A.
0339
SMITH, J.W.
0176
SMOLEN, W.F.
0075

SNAJD, V.
0227
SNODGRASS, M.J.
0174
SNYDER, D.F.
0075
SNYDER, S.H.
0315
SOKOLOV, P.P.
0144
SOLTER, D.
0317
SOROF, S.
0050
SOUF, H.D.
0166
SOULEIL, C.
0238
SPEAR, P.G.
0002
SPECTOR, F.
0119
SPIEGELMAN, S.
0141, 0142
SPOONER, T.R.
0131
SPRECHER-GOLDBERGER, S.
0187
SPRINGER, J.
0044
SPRINGER, P.
0044
SQUARTINI, F.
0192
SQUIPE, R.
0301
STANCH, G.
0140
STAMPACKY, K.M.
0318
STEINER, T.
0228
STEPHENS, R.
0175
STERN, F.
0120, 0261
STEVENS, D.
0154
STEVENS, I.C.
0304
STILLE, W.T.
0115
STILLER, D.
0085
STOCKS, P.
0280
STOKER, M.G.P.
0216
STONE, W.A.
0160
STRETT, C.S.
0301
STROHL, W.A.
0184
SUEMASU, K.
0322
SVET-MOLDAVSKY, G.J.
0057, 0144, 0145
SVORONIA, D.
0024

SVORODA, J.
 0201
 SZARD, G.
 0335*
 SZUCS, J.
 0333*
 TAKADA, M.
 0151
 TAKAHASHI, A.
 0093
 TAKAHASHI, H.
 0331
 TAKAHASHI, M.
 0095
 TAKAHASHI, T.
 0060, 0151
 TAKAYAMA, S.
 0105
 TAKIZAWA, S.
 0092
 TANI, F.
 0249
 TAROCCO, R.P.
 0342*
 TAYLOR, H.R.
 0287
 TEETS, K.
 0184
 TEIXEIRA-PINTO, A.A.
 0243*
 TERFOL, B.
 0341*
 TERAYAMA, H.
 0056
 TERNAERG, J.I.
 0042
 TERNER, J.V.
 0301*
 TERNI, M.
 0002
 THIRY, L.
 0187
 THOMAS, C.
 0031
 THORNTON, M.
 0216
 TIER, A.
 0233
 TODARIO, G.I.
 0150
 TODARO, G.J.
 0199
 TOMINGAS, R.
 0069
 TONTI, R.
 0341*
 TOOLAN, H.W.
 0210
 TORGERSEN, O.
 0064
 TOTH, R.
 0100
 TOTH, F.D.
 0335*
 TOYA, R.F., SR.
 0080
 TRAUB, F.
 0253
 TRAVNICEK, M.
 0141, 0142

TROLL, W.
 0059
 TU, S.M.
 0151
 TUTTLE, M.
 0195
 TWEEEDALE, D.M.
 0313
 TYNDALL, P.I.
 0174
 TYROLER, H.A.
 0274
 UBERTINI, T.
 0157, 0158
 UCHIKAWA, T.
 0022
 USHIJIMA, K.
 0306
 US-KRASONEC, M.
 0262*
 VACZI, I.
 0335*
 VAGNER-CARODANO, A.M.
 0343*
 VARET, D.
 0145
 VASCONCELOS-COSTA, I.
 0177
 VICKERS, P.A.
 0244
 VIGI, T.
 0251
 VIGIER, P.
 0020*
 VINCENT, P.C.
 0008
 VOGT, P.K.
 0202
 VYSHESE AVOVA, M.YA.
 0025
 WALBURG, W.F., JR.
 0174
 WALKER, K.P.
 0104
 WANG, C.H.
 0151
 WARWICK, G.P.
 0091
 WATNE, A.I.
 0228
 WATSON, F.R.
 0308
 WATSON, K.
 0141, 0142
 WATSON, T.A.
 0318
 WATTENBERG, L.W.
 0070
 WAURKE, R.
 0004
 WEE, R.
 0232
 WEEKS, J.L.
 0111
 WEIGAND, K.
 0305
 WEINSEN, U.
 0305
 WEISBURGER, J.H.
 0041, 0054

WEISS, J.F.
 0089
 WENYONG, C.F.M.
 0086, 0087
 WERTLECKI, M.
 0012
 WETTER, O.
 0226
 WHITE, A.
 0197
 WHITE, D.F.
 0318
 WHITE, J.F.
 0273
 WHITMIRE, D.F., JR.
 0301*
 WIESSER, M.
 0082
 WILLIAMS, H.R., JR.
 0054
 WINETROUT, M.
 0191
 WINTERS, D.
 0181
 WITTER, R.I.
 0161
 WIVEL, N.A.
 0171
 WOGAN, G.N.
 0046
 WOODS, W.A.
 0171
 WOODUM, J.C.
 0042
 WRIGHT, R.S.
 0175
 WYATT, A.P.
 0337*
 WYNDER, F.I.
 0286
 YAMADA, S.
 0040
 YAMAMOTO, R.S.
 0041, 0054
 YAMANE, Y.
 0096
 YANAI, R.
 0312
 YANG, C.S.
 0151
 YANG, H.Y.
 0324
 YATES, V.J.
 0182, 0208
 YOKORO, K.
 0092
 YOSHIDA, K.
 0306
 YOSHIDA, O.
 0038
 YOSHIDA, T.
 0151
 YOSHIKURA, H.
 0198
 YOSIDA, T.H.
 0098, 0102
 YOUNG, E.M.
 0050
 YU, C.K.
 0129

YU, M.
0232
ZAREZHITSKY, M.
0023
ZAIN-UL-ABEDIN, M.
0022

ZAJICEK, J.
0242*

ZAHSTRA, P.
0202

ZAPAFONETIS, C. J. D.
0310

ZAVADTI, M.
0227

ZELIJAQT, J.
0125

ZISPLATT, M.
0197

SUBJECT INDEX

- ACETOTOLUIDIDE
AMINOARENZOIC ACID, N-2-FLUORENYLACETAMIDE, CARCINOGEN-INHIBITOR (0041)
- 2-ACETYLAMINOFLUORENE
NITRITE, ANTICARCINOGEN, FREE RADICAL (0042)
- ACTINOMYCIN D
INVASIVE ABDOMINAL CARCINOMA (0024)
- ADENOCARCINOMA
BREAST CANCER, 7,12-DIMETHYLENENAN-THRACENE, ESTROGEN, RAT (0064)
CERVIX UTERI, CHROMOSOMES (0254)
COLON, CARCINOEMBRYONIC ANTIGEN, LOCALIZATION (0235)
NASAL SYSTEM, WOOD DUST (0113)
THYROID, IODINE 131 (0126)
- ADENOMA
LUNG, URETHAN, RADIATION (0101)
MALIGNANT, THYROID, X-RAY (0135)
- AFLATOXIN
B₁, LIVER NUCLEAR RNA, RNA POLYMERASE, RAT (0046)
B₂, LYMPHOCYTE TRANSFORMATION, PHYTOHEMAGGLUTININ (0045)
NUCLEIC ACID SYNTHESIS, INHIBITION (0049)
NURSING MILK, PIG, STUNTED GROWTH (0048)
TUMOR INDUCTION, NUCLEIC ACID BINDING (0047)
- AGE
ADJUSTMENT, EPIDEMIOLOGY, MATHEMATICAL MODEL (0264)
CHRONIC THYROIDITIS, RAT, TRYPAN BLUE (0034)
CORRELATION, LIVER, ALPHA-FETOPROTEIN (0231)
HODGKIN'S DISEASE, HISTOLOGY, TWO ENTITIES (0260)
INOCULATION, MOUSE MAMMARY TUMOR VIRUS, MILK ANTIGEN ASSAY (0104)
WOMEN, SURVIVAL RATE, MAMMARY CARCINOMA (0297)
- AIR POLLUTION
EPIDEMIOLOGY, LUNG CANCER (0016)
- N-ALKYL-4-AMINOAZOBENZENE
AZO DYE BINDING (0056)
- ALUMINIUM
4-NITROQUINOLINE 1-OXIDE, LUNG ADENOMA (0096)
- AMELOBLASTOMA
DENTAL CYST, RAT (0244)
- AMINOAZOTOLUENE
ORTHO-, NUCLEIC ACID BINDING, PROTEIN BINDING (0038)
- BETA-AMINOISOBUTYRIC ACID
BLADDER CARCINOMAS (0336)*
- AMINOSTILBENE
DERIVATIVES, EARLY TUMOR, TRANS-4-DIMETHYLAMINOSTILBENE (0031)
- ANTIBIOTIC
RIBOMYCIN, ORTHOAMINOAZOTOLUENE, LIVER, MOUSE (0025)
- ANTIBODY
FELINE LEUKEMIA VIRUS, VIRAL ANTIGEN (0163)
HODGKIN'S DISEASE, FR VIRUS, HERPES SIMPLEX, CYTOMEGALOVIRUS (0155)
IMMUNOGLOBULINS, IGG, IGA (0229)
MURINE SARCOMA, TUMOR-SPECIFIC ANTIGEN, 3-METHYLCOLANTHRENE (0072)
- PLATELET LEUCOCYTE, TROPHOBLASTIC TUMORS, CHORIOEPITHELIOMA (0227)
SARCOMA, VIRUS, HUMAN (0147)
SV40, PREGNANT HAMSTERS (0213)
- ANTICARCINOGEN
NITRITE, MECHANISM, FREE RADICAL, 2-ACETYLAMINOFLUORENE (0042)
- ANTIGEN
ANTIGENIC ANALYSIS, L STRAIN MOUSE CELLS, MURINE LEUKEMIA-ASSOCIATED (0165)
CARCINOEMBRYONIC, ALPHA-FETOPROTEIN, GASTROINTESTINAL TRACT CANCER, HEPATOMA, TERATOMA (0240)*
CARCINOEMBRYONIC, COLON, ADENOCARCINOMA, LOCALIZATION (0235)
EPSTEIN BARR, VIRUS ENVELOPE, LYMPHOID CELLS (0156)
ERYTHROCYTE ISOANTIGEN, VIRUS SUSCEPTIBILITY, AVIAN LEUKOSIS-SARCOMA VIRUS (0160)
GLYCOPROTEIN, MAMMARY TUMOR AGENT (0191)
IMMUNOFLOURESCENCE, ADENOVIRUS-ASSOCIATED VIRUS, HERPES VIRUS (0179)
LYMPH NODE CELLS, DNA, PHYTOHEMAGGLUTININ (0238)
MILK ANTIGEN ASSAY, MOUSE MAMMARY TUMOR VIRUS, INOCULATION AGE (0194)
RIOUS SARCOMA VIRUS COAT, HETEROKARYOTIC CELLS (0201)
SURFACE AND TUMOR, VIRUS-SPECIFIED DNA, SIMIAN VIRUS 40 (0209)
T, ADENOVIRUS-INDUCED TUMOR, FREEZING TREATMENT (0177)
TUMOR, FRIEND VIRUS, MODIFICATION (0170)
TUMOR SPECIFIC TRANSPLANTATION, ADENOVIRUS, VIRUS INDUCED TUMORS (0180)
VIRAL ANTIBODY, FELINE LEUKEMIA VIRUS (0163)
- AORTA
SWINE, HYPERLIPEMIC DIET, UNDIFFERENTIATED ENDOTHELIAL CELLS (0261)
- APIASIA
HEMATOLOGY, LEUKEMIA, BENZENE EXPOSURE, EPIDEMIOLOGY (0121)*
- ASBESTOS
MALIGNANT MESOTHELIOMA, MINING (0268)
- ATP
ATPASE ACTIVITY, HEPATOMA, PLASMA MEMBRANE OF LIVER CELLS (0259)
NUCLEAR ATPASE LOCALIZATION, MOUSE HEPATOMA (0259)
- AUTOIMMUNE DISEASE
LYMPHOPROLIFERATIVE CHANGE, GERM-FREE MICE (0149)
- BENZENE
CHROMOSOME DAMAGE, BONE MARROW (0030)
LEUKEMIA, EPIDEMIOLOGY (0121)*
- BENZ(a)PYRENE
FIBROSARCOMA, IMMUNOREACTIVITY, RNA (0222)
FIBROSARCOMA, 3-METHYLCOLANTHRENE, PROSIMIANS (0073)
HYDROXYLASE, FLAVONE, PULMONARY ADENOMA (0070)
HYDROXYLATION, INHIBITION KINETICS (0069)
3,4-BENZOPYRENE
LARYNGEAL CANCER, OCCUPATIONAL EXPO-

IURE (0117)*
 LUNG TUMORS, SILICOTIC DUSTS, RAT
 (0122)*
 RAT ETHANOL METABOLISM (0119)*
 RERYLLIUM
 EXPOSURE, LUNG CANCER (0300)*
 BLADDER
 CARCINOMAS, BETA-AMINOISOBUTYRIC ACID
 (0336)*
 PAPILLOMA, 2-NITROPHAPHTHALENE, MONKEY
 (0027)
 BLOOD
 PERIPHERAL BLOOD SMEARS, MALIGNANCY
 RELATED CYTOLOGIC CHANGES (0340)*
 BONE
 CANCER, GROWTH PEAK, PUBERTY (0314)
 EPIDEMIOLOGY, MYELOMA (0266)
 SKELETAL NEOPLASMS, ALKALINE PHOSPHA-
 TASE ACTIVITY (0327)
 BONE MARROW
 CELL COLONY, MONONUCLEAR CELL, GRANU-
 LOCYTE, STIMULATING SUBSTANCE (0328)
 CHROMOSOME DAMAGE, BENZENE (0030)
 COLONY-STIMULATING FACTOR, FACTOR
 SERUM TITER, RENAL INFLUENCE ON
 SERUM TITER, MOUSE (0332)
 IMMUNOFLOURESCENCE MICROSCOPY, ACUTE
 LEUKOSIS, ACUTE MYELOSIS, CHLOPOM
 (0233)
 BRAIN
 TUMOR, GROWTH BEHAVIOR, MATRIX
 CULTURE, HUMAN (0303)*
 TUMOR INFILTRATION, MYELIN BREAKDOWN,
 EHRLICH ASCITES TRANSPLANT, MOUSE
 (0253)
 BRUKITTIS LYMPHOMA
 AUTOIMMUNE SYSTEM, MALARIA, EPSTEIN
 BARR VIRUS (0005)
 EPSTEIN BARR VIRUS, INFECTIOUS
 MONONUCLEOSIS (0154)
 NASOPHARYNGEAL CARCINOMA, ANTIBODY
 (0151)
 SERUM ANTIBODY, NASOPHARYNGEAL CAR-
 CINOMA SERUM ANTIBODY, EPSTEIN BARR
 VIRUS (0153)
 BURSA
 BURSA LYMPHOID SYSTEM, MAREK'S
 DISEASE, HERPESVIRUS, BURSECTOMY
 (0162)
 T-BUTYL HYDROPEROXIDE
 4-QUINOLINE-1-OXIDE, FREE RADICAL,
 SQUAMOUS CELL CARCINOMA, MICE (0026)
 CANCER
 ALL SITES, MORTALITY RATES, MORBIDITY
 RATES (0279)
 CHLORNAPHAZINE, HODGKIN'S DISEASE
 (0110)
 DETECTION, PHYSICAL EXAMINATION,
 EARLY SCREENING (0295)*
 CARCINOGENICITY
 P-DIMETHYLAMINOAZOBENZENE,
 N,N-DIMETHYL-P-PHENYLAZOANILINE,
 ELECTRON DENSITY STUDIES (0029)
 GERM-FREE STATE, TUMOR PROTECTION,
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 (0045)
 MECHANISM, AFLATOXIN, NUCLEIC ACID
 SYNTHESIS (0049)
 PHENANTHRENE, DIPENZ(A,H)ANTHRACENE,
 K-REGION EPOXIDE (0067)
 CARCINOMA
 ANO-RECTAL FISTULA, PATHOGENESIS, MAN
 (0341)*
 CERVICAL SQUAMOUS CELL, POSTMENOPAUSAL
 WOMEN (0313)
 CIGARETTE TAR, LYMPHOMA, NEWBORN ICR
 MICE (0105)
 9,10-DIMETHYL-1,2-BENZANTHRACENE,
 IRRADIATION, PROLIFERATION KINETICS
 (0068)
 MAMMARY GLAND, OTHER AREAST, REVIEW
 (0014)
 NASOPHARYNX, STIRLINGS (0316)
 PENIS, PAINT, PAINT REMOVERS (0114)
 POLYP, LARGE INTESTINE, CHROMOSOME
 (0325)
 SCROTUM, INDUSTRIAL HYGIENE, OCCUPA-
 TIONAL FACTORS (0114)
 SQUAMOUS CELL, SUBMUCOUS FIBROSIS,
 PRECANCEROUS CONDITION (0247)
 CARRAGEENAN
 GRANULOMA, FREUND'S ADJUVANT (0103)
 CARTILAGE
 XIPHISTERNAL, EPITHELIOMA, INVASION
 (0250)
 CELL
 AKR-A CULTURE, LYMPHOID LEUKEMIA,
 GROSS LEUKEMIA VIRUS, MOUSE (0171)
 BHK 21 HAMSTER, DNA SYNTHESIS, POLYOMA
 VIRUS, SERUM (0214)
 CHICK EMBRYO, INTERFERON INDUCTION,
 VIRUS, ADENOVIRUS (0178)
 CHICK EMBRYO, ROUS SARCOMA VIRUS,
 SUGAR TRANSPORT (0204)
 CULTURE, MURINE SARCOMA VIRUS, MURINE
 LEUKEMIA VIRUS (0199)
 CYCLE, AUTORADIOGRAPHIC ANALYSIS,
 SOLID HUMAN TUMORS (0302)*
 CYCLE, ULTRAVIOLET IRRADIATION, MURINE
 SARCOMA VIRUS INFECTION (0198)
 EMBRYONIC, NEOPLASTIC, MINIMUM DEVI-
 ATION (0293)
 EMBRYONIC CULTURE, PAUSCHER MURINE
 LEUKEMIA VIRUS, TYPE-C VIRUS
 PARTICLE (0175)
 EPENDYMOMA, MORPHOLOGY, HUMAN (0249)
 HAMSTER EMBRYONIC, KARYOTYPE CHANGES,
 4-NITROQUINOLINE-1-OXIDE (0098)
 HETEROKARYOTIC CELLS, VIROGENIC CELL
 FUSION, ROUS SARCOMA VIRUS COAT
 ANTIGEN (0201)
 LEUKEMIC MOUSE CELL LINE, MURINE
 MYELOPROLIFERATIVE VIRUS (0166)
 LEYDIG CELL TUMOR, DIETHYLSTILBESTROL,
 DNA SYNTHESIS (0022)
 LYMPH NODE, DNA, PHYTOHEMAGGLUTININ,
 ANTIGEN (0238)
 LYMPHOBLASTIC TRANSFORMATION, PHYTO-
 HEMAGGLUTININ INDUCED, IN VITRO, MAN
 (0242)*
 LYMPHOCYTE, DEDIFFERENTIATION, PHYTO-
 HEMAGGLUTININ INDUCED, MAN (0243)*
 LYMPHOCYTE, STIMULATION, ANTIGEN,
 MELANOMA (0230)
 LYMPHOCYTE TRANSFORMATION, AFLATOXIN
 B, PHYTOHEMAGGLUTININ (0045)
 NEOPLASTIC MAST CELL, PHOSPHOLIPID
 TURNOVER (0256)
 PLASMA CELL TUMOR, FREUND ADJUVANT,
 CHROMOSOMAL ALTERATION (0102)
 RECOGNITION SITE, PROLIFERATION,
 CONTROL, LYMPHOCYTE (0008)

- SPLEEN, LYMPHOMA, MICE (0224)
 SURFACE ELECTRIC POTENTIAL, MALIGNANT CELL (0252)
 SYNGENIC LIVER, METHYLCHOLANTHRENE, TUMOR INHIBITION (0079)
 TRANSFORMATION, ONCOGENIC RNA VIRUS, REVIEW (0020)*
 YOSHIDA SARCOMA, 4-NITROQUINOLINE-1-OXIDE, CHROMOSOME ABERRATION, PERSISTENT NUCLEOLI (0097)
- CERVIX**
 CANCER, CERVICAL DYSPLASIA, ORAL CONTRACEPTIVE (0291)
 CANCER MORTALITY, CYTOLOGIC SCREENING (297)*
 CHROMOSOME, ADENOCARCINOMA (0254)
 CONE BIOPSY, EARLY CERVICAL CANCER (0248)
 MYOPLASMA, SQUAMOUS CELL (0282)
 SQUAMOUS CELL CARCINOMA, POSTMENOPAUSAL WOMEN, CYTOLOGIC FEATURES (0313)
- CHEMICAL CARCINOGENS**
 NITROSAMINES, CYSTEINE S-CARBOXY DERIVATIVES, LUNG CARCINOGENS (0083)
 PROTEIN TARGETS, PRINCIPAL PROTEIN CONJUGATES (0050)
- CHEMOTACTIC AGENT**
 MICE, HEPATOMA CELLS (0326)
- CHLORNAPHAZINE**
 HODGKIN'S DISEASE, CANCER OF THE BLADDER (0110)
- CHROMOSOME**
 ABERRATIONS, MALIGNANT TUMORS, PERIPHERAL BLOOD CULTURE (0332)
 ABERRATIONS, PAGET'S DISEASE, SIMIAN VIRUS 40 (0245)
 ABERRATIONS, YOSHIDA SARCOMA CELL, 4-NITROQUINOLINE-1-OXIDE (0097)
 ABNORMALITIES, BENZENE, BONE MARROW (0030)
 ABNORMALITIES, LARGE INTESTINE, POLYPS, CARCINOMA (0325)
 ADENOCARCINOMA OF THE CERVIX UTERI (0254)
 ALTERATION, 4-NITROQUINOLINE-1-OXIDE, 4-HYDROXYAMINOQUINOLINE-1-OXIDE, HAMSTER EMBRYONIC CELL (0098)
 ALTERATION, PLASMA CELL TUMOR, FREUND ADJUVANT (0102)
 ANOMALIES, LYMPHOBLASTIC LEUKEMIA, SYNDROME, ATYPICAL DYSGLUCINEMIA, MAN (0343)*
 BONE MARROW, 7,12-DIMETHYLBENZ(A)ANTHRACENE, LEUKEMIA (0061)
 CHRONIC LYMPHOCYTIC LEUKEMIA, TRANSLOCATION, GAMMA GLOBULIN (0234)
 DAMAGE, CYTOGENESIS, LEAD EXPOSURE (0112)
 PHILADELPHIA, ACUTE LYMPHOCYTIC LEUKEMIA (0130)
 PHILADELPHIA, CHRONIC MYELOID LEUKEMIA POLYCYTHEMIA (0010)
 RESISTANT GENE, FRIEND LEUKEMIA VIRUS (0169)
 THOROTRAST, PERIPHERAL, ABERRATIONS, LYMPHOCARCINOMA (0137)
- CIGARETTES**
 SOLID FUEL CONSUMPTION, CANCER DEATH RATES (0280)
- COLON**
 ADENOCARCINOMA, CARCINOEMBRYONIC ANTIGEN, LOCALIZATION (0235)
 CARCINOMA, FAMILIAL POLYPOSIS, HYDROLYTIC ENZYME DISTRIBUTION (0337)
 JUVENILE POLYPS, ALLERGY, FAMILIAL (0326)
 STATISTICS, HUMAN (0281)
- CYST**
 DENTAL, JAW, AMELOBLASTOMA (0244)
- CYSTEAMINE**
 CHINESE HAMSTER LUNG CELLS, IRRADIATION, MITOTIC DELAY, CHROMOSOMAL ABERRATION (0129)
- CYSTEINE S-CARBOXYL DERIVATIVES**
 NITROSAMINES, LUNG CARCINOGENS (0083)
- CYTOGENESIS**
 LEAD EXPOSURE, CHROMOSOME DAMAGE (0112)
- DESMOSTEROL**
 NERVOUS SYSTEM TUMORS, NITROSOUREA, RAT (0089)
- DIRENZ(A,H)ANTHRACENE**
 K-REGION EPOXIDE, PHENANTHRENE, DNA, RNA (0067)
- DIETARY FAT**
 TUMOR INCIDENCE, 7,12-DIMETHYLBENZ(A)ANTHRACENE, DOSE (0062)
- DIETHYLNITROSAMINE**
 LIVER CELL, NUCLEAR MEMBRANE PERMEABILITY, RAT (0081)
 SORBITOL DEHYDROGENASE, LIVER, RAT (0085)
- DIETHYLSTILBESTROL**
 DNA SYNTHESIS, LEYDIG-CELL TUMOR (0022)
- DIETHYL-SULFATE**
 NERVOUS SYSTEM TUMORS, DIMETHYL-SULFATE (0032)
- DIFFERENTIATION**
 UNDIFFERENTIATED SIRENOOTHELIAL CELLS, SWINE AORTA, HYPERLIPEMIC DIET (0261)
- 4-DIMETHYLAMINOAZOBENZENE**
 AZO DYE REDUCTASE, RAT LIVER, CECAL BACTERIA (0054)
- P-DIMETHYLAMINOAZOBENZENE**
 N,N'-DIMETHYL-P-PHENYL-AZOANILINE, CARCINOGENIC ACTIVITY, ELECTRON DENSITY STUDIES (0029)
- TRANS-4-DIMETHYLAMINOSTILBENE**
 EAR DUCT TUMOR, LEUKEMIA, RATS (0031)
- DIMETHYLBENZANTHRACENE**
 SKIN, HAMSTER, MELANOMA (0118)*
 TRYPAFLUOR, HODGKIN'S DISEASE, PATHOGENESIS, REVIEW (0019)*
- 7,12-DIMETHYLBENZANTHRACENE**
 BREAST CANCER, ESTROGEN, RAT (0064)
 DOSE, LOW FAT DIET, TUMOR INCIDENCE (0062)
 GERM-FREE STATE, TUMOR PROTECTION (0065)
 LEUKEMIA, BONE MARROW CHROMOSOME (0061)
 LIVER, ADRENAL (0066)
 MAMMARY TUMORS, HORMONE RESPONSIVENESS (0060)
 NUCLEIC ACID SYNTHESIS, LIVER REGENERATION (0058)
 PROTEASE INHIBITOR, TUMORIGENESIS PROMOTER (0059)

DIMETHYLNITROSAMINE

7,12-DIMETHYLBENZ(A)ANTHRACENE,
 MOUSE LIVER MORPHOLOGY (0081)
 LUNG ADENOMA, LIVER HEMANGIOSARCOMA
 (0080)
 RNA METHYLATION, S-ADENOSYLMETHIONINE,
 RAT LIVER (0082)

DIMETHYL-SULFATE

DIMETHYL-SULFATE, NERVOUS SYSTEM TUMORS
 (0032)

2,5-DIMETHOXY-4-AMINOAZOBENZENE

HEPATOMA, TARGET ORGANS, DOSE EFFECT,
 RAT (0055)

DNA

CROWN-GALL TISSUE CULTURE, MODEL,
 TRANSFORMATION MECHANISM (0263)*
 LYMPH NODE CELLS, PHYTOHEMAGGLUTININ,
 ANTIGEN (0238)
 POLYMERASE, DNA-DIRECTED, VIRUS
 (0141)
 POLYMERASE, HUMAN UROGENITAL TUMOR
 (0331)
 POLYMERASE, RNA HYBRID, ONCOGENIC
 VIRUS (0142)
 POLYMERASE TEMPLATE, SARCOMA-LEUKEMIA,
 VIRAL DNA-DNA HYBRID MOLECULE
 (0143)
 POLYOMA VIRUS, AT-TYPE FIBROSARCOMA,
 GC-TYPE ADENOCARCINOMA (0220)
 ROUS SARCOMA VIRUS, ISOLATION (0203)
 SYNTHESIS, DENSONUCLEOSIS VIRUS,
 ONCOGENICITY (0221)*
 SYNTHESIS, LEYDIG-CELL TUMOR,
 DIETHYLSTILBESTROL (0221)
 SYNTHESIS, PARVOVIRUS H-1, SV40,
 THYMIDINE KINASE (0210)
 SYNTHESIS, VIRUS, SERUM (0216)
 VIRUS-SPECIFIED, SV40, SURFACE AND
 TUMOR ANTIGENS (0209)

DUODENUM

DIETETIC PANTHENTIC ACID DEFICIENCY,
 FOCAL AVILLIOUS HYPERPLASIA, MOUSE
 (0311)

DUST

SILICOTIC, EFFECT ON 3,4-BENZOPYRENE
 INDUCING OF LUNG TUMORS, RAT (0122)*

FAP

DUCT TUMOR, LEUKEMIA, AMINOSTILBENE
 DERIVATIVES (0031)

EARLY SCREENING

CANCER DETECTION, PHYSICAL EXAMINATION
 (0295)*

ELECTROPHORESIS

POLYOMA VIRUS, TRANSFORMED CELL LINES
 IN VIVO, HAMSTER (0215)
 SALIVARY GLAND NEOPLASM, ENVIRONMENT,
 VITAMIN A, RAT (0308)
 SKIN GRAFT, TUMOR, HETEROGENIZATION
 (0057)
 SUPPLEMENTARY ASSAY, NEOPLASM (0063)

7,10-DIMETHYL-1,2-BENZANTHRACENE

SQUAMOUS CELL CARCINOMA, PROLIFERATION
 KINETICS, IRRADIATION (0068)

3,3'-DIMETHYLBENZIDINE

SKIN TUMORS, SERACEOUS GLAND, RAT
 (0023)

1,2-DIMETHYLHYDRAZINE

INTESTINAL CARCINOMA, EARLY STAGES,
 AUTORADIOGRAPHY (0044)

ENVIRONMENTAL FACTOR

CERVIX, HERPES-SIMPLEX TYPE-2 (0187) ENZYME

ACID AND ALKALINE PHOSPHATASE,
 LACTIC AND GLUCOSE-6-PHOSPHATE
 DEHYDROGENASE, LUNG (0127)
 ALKALINE PHOSPHATASE ACTIVITY,
 SKELETAL NEOPLASMS (0327)
 ARYL HYDROLASE, BENZO(A)PYRENE
 HYDROXYLATION, INHIBITION KINETICS,
 IN VITRO (0049)
 ATO DYE REDUCTASE, LIVER, CECAL
 BACTERIA, RAT (0054)
 BENZO(A)PYRENE HYDROXYLASE, FLAVONE
 INDUCER, PULMONARY ADENOMA (0070)
 DIETARY INDUCTION, HEPATOCARCINOGENS,
 3-METHYL-4-DIMETHYLAMINOAZOBENZENE
 (0052)
 DIETARY INDUCTION, 3-METHYL-4-
 DIMETHYLAMINOAZOBENZENE, 2-METHYL-4-
 DIMETHYLAMINOAZOBENZENE (0051)
 DNA POLYMERASE, HUMAN UROGENITAL TUMOR
 (0331)
 GLUCOSE-6-PHOSPHATE DEHYDROGENASE
 ISOZYMES, LIVER, RHODAMINE SARCOMA,
 RAT (0035)
 HEXOKINASE, HEPATIC TUMOR, GROWTH RATE
 (0288)
 HYDROLYTIC, CARCINOMA OF COLON,
 FAMILIAL POLYPOSIS (0337)*
 LACTATE DEHYDROGENASE, 6-PHOSPHO-
 GLUCONATE DEHYDROGENASE, PHOSPHO-
 HEXOSE ISOMERASE, BREAST CARCINOMA
 (0330)*
 MURAMIDASE, POLYCYTHEMIA VERA,
 GRANULOCYTE (0320)
 NONSPECIFIC ESTERASE, ACID PHOSPHA-
 TASE, MALIGNANT LYMPHOPROLIFERATIVE
 DISEASE (0257)
 ORNITHINE DECARBOXYLASE, THIOACETAMIDE
 RNA METABOLISM (0039)
 ORNITHINE DECARBOXYLASE ACTIVITY,
 HEPATOMA, SARCOMA (0315)
 PROTEASE INHIBITORS, TUMORIGENESIS
 PROMOTERS, 7,12-DIMETHYLBENZ(A)
 ANTHRACENE (0059)
 SERUM ALKALINE PHOSPHATASE, HODGKIN'S
 DISEASE, ISOZYMES (0246)
 SORBITOL DEHYDROGENASE, DIETHYLNITRO-
 SAMINE CARCINOGENESIS, LIVER, RAT
 (0085)
 THYMIDINE KINASE, SV40, DNA SYNTHESIS,
 PARVOVIRUS H-1 (0210)
 T-RNA METHYLASE, POLYOMA VIRUS (0217)
 EPENDYMOMA
 AVIAN ADENOVIRUS, CHICKEN-EMBRYO
 LETHAL-ORPHAN (0182)
 MORPHOLOGY, POLYGONAL CRYSTALLINE
 STRUCTURE (0249)
 EPIDEMIOLOGY
 BAVARIA, LEUKEMIA MORTALITY (0270)
 BENZENE EXPOSURE, LEUKEMIA (0121)*
 BREAST CANCER, HUMAN, CANINE (0277)
 CANCER, BREAST, GENITAL ORGANS,
 FEMALE, QUEBEC (0298)*
 CYTOLOGIC SCREENING, CERVICAL CANCER
 MORTALITY (0297)*
 GALLBLADDER CANCER, WORLD INCIDENCE,
 ETIOLOGY (0018)*
 HODGKIN'S DISEASE, GERMANY (0272)
 HODGKIN'S DISEASE, JAPAN (0271)
 INCIDENCE, AGE-ADJUSTMENT, FINLAND

- (0264)
LEUKEMIA, CNS, CHILDREN, INCREASE
(0283)
LEUKEMIA, SEX MORTALITY RATIO (0275)
LUNG CANCER, AIR POLLUTION (0016)
SALIVARY GLAND TUMORS, EASTERN
GERMANY, MALIGNOMAS, POLYMORPHIC
ADENOMAS (0285)
SPACE-TIME CLUSTERING, LEUKEMIA,
CHILDREN (0278)
SUGAR AND FAT INTAKE, BREAST CANCER,
BLOOD GROUP A (0265)
EPIDERMIS
BIOELECTROMETRIC MEASUREMENT,
3-METHYLCHOLANTHRENE, MOUSE (0075)
EPIPHARYNX
EPITHELIAL CARCINOMA, PETICULAR CELL
SARCOMA, REVIEW (0013)
EPITHELIOMA
INVASION, XIPHISTERNAL CARTILAGE
(0250)
SMALLPOX VACCINE SCARS, MAN (0339)
EPITHELIUM
CARCINOMA, RETICULAR CELL SARCOMA,
EPIPHARYNGEAL CANCER (0013)
MOUSE CHLODENDUM, GAMMA-RADIATION,
CELL PRODUCTION (0123)
ERGOCORININE
2-RR-ALPHA-ERGOKRYPTIN, MAMMARY
HYPERPLASTIC NODULES, PROLACTIN,
MICE (0312)
ETHYL-NITROSOUREA
NEUROGENIC MALIGNANCIES (0090)
ETIOLOGY
NONGONADAL NEOPLASM, TURNER'S SYNDROME
(0012)
SKIN CANCER, CHRONIC LYMPHOCYTIC
LEUKEMIA (0318)
EYE LID
BASAL CELL CARCINOMA (0274)
FACTOR
RENAL INFLUENCE ON SERUM TITER, BONE
MARROW COLONY-STIMULATING FACTOR,
MICE (0332)
FAMILIAL POLYPOSIS
HYDROLYTIC ENZYME DISTRIBUTION,
CARCINOMA OF COLON (0337)
FANCONI'S ANEMIA
MYELOMONOCYTIC LEUKEMIA, CHROMOSOME,
VIRUS (0150)
FIBROSARCOMA
AT-TYPE, GC-TYPE ADENOCARCINOMA,
POLYOMA VIRUS, DNA (0220)
BENZ(A)PYRENE, RNA, IMMUNOREACTIVITY
(0222)
3-METHYLCHOLANTHRENE, BENZO(A)PYRENE,
PROSIMIANS (0073)
FIBROSIS
SQUAMOUS, PRECANCEROUS CONDITION,
SQUAMOUS CELL CARCINOMA (0247)
FLAVONE
PULMONARY ADENOMA, BENZO(A)PYRENE
HYDROXYLASE ACTIVITY (0070)
N-2-FLUORENYLACETAMIDE
CARCINOGEN-INHIBITOR, ACETOTOLUIDIDE
ISOMERS, AMINOBENZOTIC ACID (0041)
N,N'-2,7-FLUORENYLBIURETACETAMIDE
HEPATOMA, X-RADIATION, ACCELERATED
INDUCTION (0040)
FORMIC ACID 2-(4-(5-NITRO-2-FURYL)-2-
THIAZOLYL) HYDRAZIDE
RENAL CARCINOMAS (0037)
FREUND ADJUVANT
CHEMICAL CARCINOGENS, CHROMOSOMAL
ALTERATION, PLASMA CELL TUMOR (0102)
GRANULOMA, CARPAGEFMAN (0103)
GALLBLADDER
URINARY TRACT, N-(4-(5-NITRO-2-FURYL)-
2-THIAZOLYL)FORMAMIDE, N-(4-(5-NITRO-
2-THIAZOLYL)ACETAMIDE, CARCINOGENI-
CITY (0038)
GANGLIONEUROMA
NEUROBLASTOMA, TURNER'S SYNDROME,
NONGONADAL NEOPLASIA (0012)
GASTROINTESTINAL TRACT
AND-RECTAL FISTULA, MALIGNANT TRANS-
FORMATION, CARCINOMA (0341)
GALLBLADDER CANCER, EPIDEMIOLOGY,
ETIOLOGY (0018)
GASTRIC STUMP, PRIMARY CANCER, ULCER
DISEASE GASTRECTOMY, MAN (0140)
GENETICS
SKIN HETEROGENIZING VIRUS, STRAIN
SPECIFIC VIRUS (0145)
SUSCEPTIBILITY TO LEUKEMIA INDUCTION,
AKR THYMUS GRAFT, GROSS VIRUS
(0172)
TWIN PAIR, SMOKING, LUNG CANCER
MORTALITY (0109)
GLUCOSE
METABOLISM, CANCER BIOCHEMISTRY,
REVIEW (0007)
GRANULOCYTE
KINETIC STUDY, ACUTE MYELOMONOCYTIC
LEUKEMIA, ACUTE MYELOGENOUS
LEUKEMIA (0290)
POLYCYTHEMIA VERA, MURAMIDASE (0320)
GRANULOMA
CAPRAGEFMAN, FREUND'S ADJUVANT (0103)
GROWTH
BEHAVIOR, MATRIX CULTURE, HUMAN
BRAIN TUMOR (0303)
CHARACTERISTICS, SICR-PRC DILUTION,
ASCITIC PLASMACYTOMA (0291)
FACTOR, BONE MARROW, BLOOD FACTOR
(0328)
INTESTINAL TUMORS,
1,2-DIMETHYLHYDPAZINE, AUTORADI-
OGRAPHY (0044)
RATE, HEYOKINASE, HEPATIC TUMOR
(0288)
RATE, MORRIS HEPATOMA, MINIMUM
DEVIATION (0293)
SOLID HUMAN TUMORS, CELL CYCLE, AUTO-
RADIOGRAPHIC ANALYSIS (0302)
HEART
FIBROBLAST CELL CULTURE, ADENOVIRUS,
RABBIT (0181)
HEMAGGLUTINATION
INHIBITOR ADENOVIRUS, SPECIFICITY
(0183)
HEPATOMA
CHEMOTACTIC AGENT, MICE (0300)
MORRIS, EMPYONIC IMPLANT, MINIMUM
DEVIATION (0293)
MORRIS, TOTAL PROTEIN SYNTHESIS,
ALBUMIN SYNTHESIS (0305)
ORNITHINE DECARBOXYLASE ACTIVITY
(0315)
PLASMA MEMBRANE OF LIVER CELLS,
ATPASE ACTIVITY (0258)
HETEROGENIZATION

SKIN, GRAFT, TUMOR (0057)
TAMINE
WHOLE BODY IRRADIATION, SKIN LESIONS,
RAT (0139)*
TOGENESIS
MIXED TUMOR, SALIVARY GLAND, HUMAN
(0251)
SKIN'S DISEASE
AGE, HISTOLOGY (0260)
CANCER OF THE BLADDER, CHLORNAPHAZINE
(0110)
EPSTEIN BARR VIRUS, HERPES SIMPLEX,
CYTOMEGALOVIRUS, ANTIBODY (0155)
GERMANY, EPIDEMIOLOGY (0272)
JAPAN, EPIDEMIOLOGY (0271)
SERUM ALKALINE PHOSPHATASE, ISOZYMES,
HODGKIN'S LYMPH NODE (0246)
SPONTANEOUS, CHEMICALLY INDUCED,
ANIMALS, MAN, PATHOGENESIS, REVIEW
(0019)*
NONE
ESTRADIOL-17 BETA, LYMPHOID CELL
PROLIFERATION, IN VITRO, LYMPHO-
SARCOMA, ACUTE LYMPHOBLASTIC
LEUKEMIA, MAN (0342)*
RESPONSIVENESS, 7,12-DIMETHYLBENZ(A)
ANTHRACENE, MAMMARY TUMORS (0060)
RAZINE
TOXICITY IN PREGNANT RATS (0043)
ERPLASIA
FOCAL AVILLOUS, MOUSE DUODENUM,
DIETETIC PANTHENTIC ACID DEFICIENCY
(0311)
OXIA
POLYCYTHEMIA, TRANSFUSION, ERYTHRO-
POIETIN (0307)
UNITY
ALLOGRAFT SURVIVAL, X-IRRADIATION,
MOUSE LEUKEMIA CELLS (0225)
AUTOIMMUNE RESPONSE, LYMPHOID
NEOPLASIA, REVIEW (0009)
RNA-TRANSFERRED, 3-METHYLCOLANTURENE,
LIPOSARCOMA (0077)
IMMUNOFLOURESCENCE
MICROSCOPY, BONE MARROW, ACUTE
LEUKOSIS, ACUTE MYELOSIS, CHILDREN
(0233)
IMMOBILIZATION
IGG, MYELOMA, LIGHT AND HEAVY POLY-
PEPTIDE CHAINS (0226)
LIVER, CARCINOMA, CIRRHOSIS (0232)
TUMOR, IGG, IGA (0229)
INOLOGY
BURKITT'S LYMPHOMA, NASOPHARYNGEAL,
CARCINOMA (0151)
GENITAL HERPES SIMPLEX VIRUS, ANTI-
BODIES, HUMAN CERVIX CARCINOMA
(0186)
LYMPHOMA, INACTIVATION, RADIATION,
MOUSE (0223)
MELANOMA, LYMPHOCYTE STIMULATION,
TUMOR EXTRACT (0230)
NEOPLASM, MACROPHAGE MIGRATION,
DELAYED HYPERSENSITIVITY REACTION
(0228)
MOTHERAPY
POLYOMA VIRUS INDUCED, U.V. IRRADIA-
TION, EXTRACT, HAMSTER (0241)*
INFECTION MONONUCLEOSIS
BURKITT'S TUMOR, EPSTEIN BARR VIRUS
(0154)

INFILTRATION
EHRlich ASCITES TRANSPLANT, MYELIN
BREAKDOWN, BRAIN, WHITE MOUSE
(0253)
INFRARED EMISSION
PAPILLOMA (0334)*
INHIBITOR
HERPES VIRUS, GIANT CELL FORMATION,
RABBIT KIDNEY, COMPOUND 48/80
(0188)
INTERFERON
ENDOGENEOUS, DEFENSE AGAINST ONCOGENIC
VIRUSES, REVIEW (0021)*
INDUCTION, CHICK EMBRYO CELLS, ADENO-
VIRUS, VIRUS (0178)
LEUKEMIA, LEUKOCYTES (0335)*
INTESTINE
1,2-DIMETHYLHYDRAZINE, CARCINOMAS,
PAPILLOMAS (0044)
INTESTINE, LARGE
CARCINOMA, POLYP, CHROMOSOME (0325)
IODINE 131
THYROID, PAPILLARY ADENOCARCINOMA
(0126)
IRAN
EPIDEMIOLOGY, CERVIX, SKIN, BREAST
(0284)
ISOPROTERENOL
CYTOPLASMIC RNA SYNTHESIS, CELL
PROLIFERATION (0309)
JAM
AMELOBLASTOMA, DENTAL CYST (0244)
KERATOSIS
SOLAR, SKIN CANCER, EXPOSURE TO
SUNBURN (0269)
KIDNEY
FEMAL CARCINOMAS, FORMIC ACID 2-(4-(5-
NITRO-2-FURYL)-2-THIAZOLYL)HYDRAZIDE
(0037)
KINETICS
SIMIAN VIRUS 40, NEOPLASM, HUMAN,
HAMSTER (0289)
LACTATION
PREGNANCY, BREAST CANCER (0321)
LARYNX
OCCUPATIONAL EXPOSURE, 3,4-BENZOPYRENE
(0117)*
LEAD
CHROMOSOME DAMAGE, CYTOGENESIS (0112)
LEUKEMIA
ACUTE LYMPHOCYTIC, PHILADELPHIA
CHROMOSOME (0130)
ACUTE MYELOMONOCYTIC, ACUTE MYELOGE-
NOUS, GRANULOCYTE KINETIC STUDY
(0290)
BLOOD DYSCRASIA, IMMUNITY, MYCOPLASMA
(0310)
BURKITT'S LYMPHOMA, INFECTIOUS MONO-
NUCLEOSIS, EPSTEIN BARR VIRUS
(0004)
CNS, CHILDREN, INCIDENCE (0283)
CHILDREN, SPACE-TIME CLUSTERING,
SAN FRANCISCO (0278)
CHRONIC LYMPHOCYTIC, A1/G CHROMOSOME,
GAMMAGLOBULIN (0234)
CHRONIC LYMPHOCYTIC, SKIN CANCER,
ETIOLOGY (0318)
CHRONIC MYELOID, POLYCYTHEMIA,
PHILADELPHIA CHROMOSOME (0010)
7,12-DIMETHYLBENZ(A)ANTHRACENE, BONE
MARROW CHROMOSOME (0061)

- GENETIC SUSCEPTIBILITY, GROSS VIRUS, THYMUS GRAFT (0172)
IMMUNOFLOUORESCENCE MICROSCOPY, BONE MARROW, CHILDREN (0233)
LEUKOCYTES, INTERFERON PRODUCTION (0335)*
LYMPHOID, AKR-A CULTURE, GROSS LEUKEMIA VIRUS, MOUSE (0171)
MOLONEY LEUKEMIA VIRUS, PREDNISOLONE, THYMUS (0173)
MORTALITY, RAVARIA (0270)
MOUSE LEUKEMIA CELLS, ALLOGRAFT SURVIVAL, X-IRRADIATION (0225)
MURINE LEUKEMIA-ASSOCIATED ANTIGEN, ANTIGENIC ANALYSIS, L STRAIN MOUSE CELLS (0165)
MYELOMONOCYTIC, FANCONI'S ANEMIA, CHROMOSOME, VIRUS (0150)
N-NITROBUTYLUREA (0091)
N-NITROSOPUTYLUREA, MAMMARY TUMOR, MICE, RATS (0092)
SEX MORTALITY RATIO, EPIDEMIOLOGY (0275)
SPONTANEOUS, FISCHER RAT, PATHOLOGY (0323)
VIRUS-LIKE PARTICLES, BONE MARROW CELLS, HERPES SIMPLEX VIRUS (0149)
LEUKOCYTE
INTERFERON PRODUCTION, LEUKEMIA (0335)*
LIPIDS
ALTERED, HEWT TEST, NECROSIS (0036)
LIPOSARCOMA
RNA-TRANSFERRED IMMUNITY, 3-METHYL-CHOLANTHRENE (0077)
LIVER
AFATOXIN B, NUCLEAR RNA, RNA POLYMERASE, RAT (0044)
AZO DYE BINDING, N-METHYL-4-AMINO-AZOBENZENE (0056)
CARCINOMA, ALPHA-FETOPROTEIN, GI CANCER, CARCINOEMBRYONIC ANTIGEN (0240)*
CARCINOMA, CIRRHOSIS, IMMUNOGLOBULIN (0232)
CELL, NUCLEAR MEMBRANE PERMEABILITY, DIETHYLNITROSAMINE, RAT (0084)
CHROMATIN TEMPLATE ACTIVITY, 3-METHYL-CHOLANTHRENE (0071)
CULTURE, 4-NITROQUINOLINE-1-OXIDE, ULTRASTRUCTURE, RAT (0094)
DIETHYLNITROSAMINE, SORBITOL DEHYDROGENASE, RAT (0085)
ALPHA-FETOPROTEIN, AGE CORRELATION (0231)
HEMANGIOSARCOMA, DIMETHYLNITROSAMINE, LUNG ADENOMA (0080)
HEPATOMA, GROWTH RATE, HEXOKINASE (0288)
HEPATOMA, N,N'-2,7-FLUORENYLENE-BISACETAMIDE, X-IRRADIATION (0040)
3-METHYL-4-DIMETHYLAMINOAZOBENZENE, DIETARY INDUCTION OF ENZYMES (0052)
7-METHYLBENZ(A)ANTHRACENE METABOLISM, ADRENAL, 7,12-DIMETHYLBENZ(A)-ANTHRACENE (0066)
MOUSE HEPATOMA, NUCLEAR ATPASE LOCALIZATION (0259)
ORTHODIAMINOAZOTOLUENE, RIBOMYCIN, MOUSE (0025)
REGENERATION, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, NUCLEIC ACID SYNTHESIS (0059)
SYNGENIC CELLS, 3-METHYLCHOLANTHRENE, TUMOR INHIBITION (0079)
TUMORS, 4-AMINOAZOBENZENE DERIVATIVES, TARGET ORGANS, DOSE EFFECT, RAT (0055)
ULTRASTRUCTURE, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, DIMETHYLNITROSAMINE (0081)
LUNG
ADENOMA, ALUMINIUM, 4-NITROQUINOLINE 1-OXIDE (0086)
ADENOMA, BENZO(A)PYRENE HYDROXYLASE ACTIVITY, FLAVONE INDUCER (0070)
ADENOMA, LIVER HEMANGIOSARCOMA, DIMETHYLNITROSAMINE (0080)
ADENOMA, URETHAN, RADIATION (0101)
BRONCHIAL CARCINOMA, CIGARETTE SMOKING, REAGLE (0108)
CANCER, AIR POLLUTION, EPIDEMIOLOGY (0036)
CANCER, BERYLLIUM EXPOSURE (0300)*
CANCER, CIGARETTE SMOKING, EPIDEMIOLOGY (0286)
CANCER, HEMATITE MINING (0035)
CANCER, MORTALITY RATES, SMOKING (0017)
CANCER MORTALITY, SMOKING, TWIN PAIR (0109)
CARCINOMA, METASTASIS PATTERN, YOSHIDA ASCITES SARCOMA (0322)
CURSCHMANN SPIRAL, CIGARETTE SMOKING (0104)
GOAT, PULMONARY MUCOEPIDERMOID TUMOR (0301)*
HISTOCHEMISTRY, WHOLE BODY IRRADIATION, RAT (0127)
NITROSAZETIDINE, NITROSOMETHA-METHENEMINE, STOMACH (0084)
OIL MIST EXPOSURE, RESPIRATORY TRACT CANCER (0276)
PULMONARY ISCHEMIA, IONIZING IRRADIATION (0124)
TUMORS, 3,4-BENZOPYRENE, EFFECT OF SILICOTIC DUSTS, RAT (0122)*
TUMORS, CYSTEINE S-CARBOXYL DERIVATIVE, NITROSAMINES (0083)
ULTRASTRUCTURE, WHOLE BODY IRRADIATION, RAT (0128)
LYMPHOCYTE
PROLIFERATION, CONTROL, RECOGNITION SITE (0008)
TRANSFORMATION, CYCLIC AMP, PHYTO-HEMAGGLUTININ (0236)
TRANSFORMATION, LYMPHOMAS, PHYTO-HEMAGGLUTININ, CELL CULTURE (0239)
LYMPHOMA
BIRKITT'S, MALARIA, AFRICA (0006)
DIFFERENTIAL GEOGRAPHIC PREVALENCE, MULTIPLE MYELOMAS (0267)
INACTIVATION, IRRADIATION, IMMUNOLOGY, MOUSE (0223)
LEUKEMIA, AUTOIMMUNE RESPONSE (0009)
MALIGNANT, METHYLNITROSOURFA, DOSE AND SCHEDULE EFFECT, MICE (0088)
MALIGNANT LYMPHOPROLIFERATIVE DISEASE, ACID PHOSPHATASE ACTIVITY, NONSPECIFIC ESTERASE ACTIVITY (0257)
MICE, SPLEEN CELL (0224)

- LYMPHOMYELOMA
RADIUM POISONING, OSTEOSARCOMA (0001)
LYMPHOPROLIFERATIVE SYNDROME
ATYPICAL DYSGLORINEMIA, CHROMOSOMAL
ANOMALIES (0343)*
- LYMPHOSARCOMA
ACUTE LYMPHOBlastic LEUKEMIA,
LYMPHOID CELL PROLIFERATION IN
VITRO, ESTRADIOL-17 BETA, MAN
(0342)*
EPSTEIN BARR VIRUS, JUVENILE BURKITT
LYMPHOMA, NECK, GERMANY (0152)
THYMUS-INDEPENDENT, PREDNISOLONE,
MURINE LYMPHOMA VIRUS (0167)
- MACROPHAGE
MIGRATION, DELAYED HYPERSENSITIVITY
REACTION, TUMOR IMPLANT (0229)
- MALARIA
BURKITT'S LYMPHOMA, AFRICA (0006)
BURKITT'S LYMPHOMA, EPSTEIN BARR
VIRUS, AUTOIMMUNE SYSTEM (0005)
- MAMMARY GLAND
ADENOCARCINOMA, 7,12-DIMETHYLBENZ-
ANTHRACENE, ESTROGEN INTERACTION,
RAT (0064)
ADENOCARCINOMA, NUCLEIC ACID ESTIMA-
TION, BASIC PROTEIN ESTIMATION
(0190)
CANCER, EPIDEMIOLOGY, HUMAN, CANINE
(0277)
CANCER, EPIDEMIOLOGY, QUEBEC (0298)*
CANCER, LACTATION, PREGNANCY (0321)
CANCER, MORBIDITY RATES IN HUNGARY
(0294)*
CANCER, SUGAR AND FAT INTAKE, BLOOD
GROUP A (0265)
CARCINOMA, ACIDIC NUCLEAR PROTEINS,
ENZYME ACTIVITY (0338)*
CARCINOMA, OTHER BREAST, REVIEW
(0014)
CARCINOMA, WOMEN, SURVIVAL RATE (0287)
CERVIX, SKIN, IRAN, EPIDEMIOLOGY
(0284)
DOUBLE MALIGNANCY, UTERUS (0299)*
HYPERPLASTIC NODULES, ERGOCORININE,
2-AR-ALPHA-ERGOKRYPTIN, MICE (0312)
NODULE OUTGROWTH LINE D BALB/C,
MAMMARY TUMOR VIRUS, METHYLCHOL-
ANTHRENE (0076)
TUMOR, ASPIRATION BIOPSY, CYTOLOGIC
DIAGNOSIS (0262)*
TUMOR, HORMONE RESPONSIVENESS,
7,12-DIMETHYLBENZ(A)ANTHRACENE
(0060)
TUMOR, N-NITROSODIETHYLUREA, LEUKEMIA,
MICE, RATS (0092)
TUMOR, SPLENECTOMY, THYMECTOMY,
URETHAN (0099)
TUMOR, VIRUS PARTICLE, ELECTRON
MICROSCOPIC STUDY (0146)
TUMOR VIRUS, FOSTER-NURSING, TRANS-
MISSION (0193)
TUMORIGENESIS, THYMECTOMY, INFLUENCE
OF MOUSE STRAIN (0192)
- MAPK'S DISEASE
HERPES VIRUS, INFECTIVITY, ANTIGEN
(0157)
PERIPHERAL NERVE LESIONS, RETICULO-
ENDOTHELIOSIS VIRUS (0161)
SCIATIC NERVE LESION (0158)
VIRUS, HERPES VIRUS, BURSECTOMY (0162)
- VIRUS, HERPES VIRUS CAL-1, BLADDER
TYPE, TISSUE CULTURE (0159)
- MASTOCYTOMA
CANINE, MUCOSUBSTANCES (0329)
- MELANOMA
RIA, SPONTANEOUS, METASTASIS, MOUSE
(0078)
DIMETHYLBENZANTHRACENE, SKIN,
HAMSTER (0118)*
TUMOR EXTRACT, LYMPHOCYTE STIMULATION,
IMMUNOLOGY (0230)
- MEMBRANE
MALIGNANT CELL, CELL SURFACE ELECTRIC
POTENTIAL (0252)
PLASMA, LIVER CELLS, HEPATOMA, ATPASE
ACTIVITY (0258)
- MESOTHELIOMA
ABDOMINAL CARCINOMA, ACTINOMYCIN D
(0074)
ASBESTOS EXPOSURE (0268)
- METABOLISM
ABERRATION, ENDOCRINE DISEASES,
MALIGNANCIES (0011)
GLUCOSE, CANCER BIOCHEMISTRY, REVIEW
(0007)
- METASTASIS
20-METHYLCHOLANTHRENE, MELANOMA RIA,
SARCOMA (0078)
YOSHIDA ASCITES SARCOMA, LUNG
CARCINOMA (0322)
3-METHOXY-4-AMINOAZOBENZENE
HEPATOMA, TARGET ORGANS, DOSE EFFECT
(0055)
- METHYLATION
TRNA, HYPERMETHYLATION, DIMETHYLSUL-
FATE (0319)
- 2-METHYL-4-DIMETHYLAMINOAZOBENZENE
ENZYME DIETARY INDUCTION (0051)
3-METHYL-4-DIMETHYLAMINOAZOBENZENE
DIETARY INDUCTION OF ENZYMES, HEPATO-
CARCINOGEN (0052)
ENZYME DIETARY INDUCTION (0051)
LIVER H PROTEIN, MOUSE (0053)
N-METHYL-N'-NITRO-N-NITROSOGUANIDINE
STOMACH, ULCERS, CANCER (0093)
7-METHYLBENZ(A)ANTHRACENE
LIVER, ADRENAL (0066)
METHYLCHOLANTHRENE
MAMMARY TUMOR VIRUS, NODULE OUTGROWTH
LINE D BALB/C (0076)
SKIN SUSCEPTIBILITY, CIRCADIAN RHYTHM,
MITOSIS, MICE (0074)
3-METHYLCHOLANTHRENE
FIBROSARCOMA, BENZO(A)PYRENE, PRO-
SIMIANS (0073)
INTERACTION WITH MOUSE EPIDERMIS,
BIOELECTROMETRIC MEASUREMENT (0075)
LIPOSARCOMA, RNA TRANSFERRED IMMUNITY
(0077)
LIVER CHROMATIN TEMPLATE ACTIVITY
(0071)
MURINE SARCOMA, TUMOR SPECIFIC ANTIGEN
(0072)
RAT ETHANOL METABOLISM (0119)*
SARCOMA, METASTASIS, MOUSE (0078)
SYNGENIC LIVER CELLS, TUMOR INHIBITION
(0079)
- METHYLNITROSOUREA
MALIGNANT LYMPHOMA, DOSE AND SCHEDULE
EFFECTS, MICE (0088)

MITOSIS
MOUSE DUODENAL EPITHELIUM, GAMMA-IRRADIATION (0123)

MORBIDITY
CANCER, ALL SITES, MORTALITY RATES (0279)

MORPHOLOGY
MALIGNANCY RELATED CYTOLOGIC CHANGES, PERIPHERAL BLOOD SMEARS (0340)*
SARCOMA, AVIAN LEUKOSIS, CELL PARTICLE (0324)

MORTALITY
CANCER MORTALITY DATA, NON-PUEERTO RICAN WHITE POPULATION, NEW YORK CITY (0296)*
RATES, MORBIDITY RATES, CANCER, ALL SITES (0279)

MYCOPLASMA
CERVIX, SQUAMOUS CELL (0282)
LEUKEMICS, BLOOD DYSCRASIAS, IMMUNITY (0310)

MYELOMA
EPIDEMOLOGY, BONE (0266)
G-TYPE IMMUNOGLOBULINS, LIGHT AND HEAVY POLYPEPTIDE CHAINS (0226)
MULTIPLE, LYMPHOMA, GEOGRAPHICAL ASPECTS (0267)
MULTIPLE, PARAPROTEIN, ELECTROPHORESIS (0333)*

NASOPHARYNX
CARCINOMA, BURKITT'S LYMPHOMA, ANTI-BODY (0151)
CARCINOMA, SIBLINGS (0316)
CARCINOMA SERUM ANTIBODY, EPSTEIN BARR VIRUS, BURKITT'S LYMPHOMA SERUM ANTIBODY (0153)

NECRO
FIBROUS TISSUE SARCOMA, SOFT TISSUE SARCOMA (0273)

NEOPLASM
7,12-DIMETHYLBENZ(A)ANTHRACENE, SUPPLEMENTARY ASSAY (0063)
EPITHELIOMA, SMALLPOX VACCINE SCARS, MAN (0339)*
OCCUPATIONAL HAZARD, OIL MIST EXPOSURE (0115)
PRIMARY CANCER, GASTRIC STUMP, ULCER DISEASE GASTRECTOMY, MAN (0140)*
TERPHEHYL, REACTOR COOLANT (0111)

NERVE
PERIPHERAL LESIONS, RETICULENDOTHELIOSIS VIRUS, MAREK'S DISEASE (0161)
SCIATIC NERVE LESION, MAREK'S DISEASE (0158)

NERVOUS SYSTEM
DIMETHYL-SULFATE, DIETHYL-SULFATE, TUMORS (0032)
MALIGNANCY, ETHYL-NITROSOUREA (0090)
TUMORS, NITROSOUREA, DESMOSTEROL (0080)

NEUROBLASTOMA
GANGLIONEUROMA, TURNER'S SYNDROME, NONGONADAL NEOPLASIA (0012)

NEUT TEST
NECROSIS, ALTERED LIPIDS (0036)

NITRITE
FREE RADICAL, ANTICARCINOGEN, 2-ACETYLAMINOFLUORENE (0042)

N-(4-(5-NITRO-2-FURYL)-2-THIAZOLYL) FORMAMIDE
UPINARY CARCINOGENICITY, GALL BLADDER (0038)

2-NITRONAPHTHALENE
BLADDER PAPILLOMA, MONKEY (0027)

4-NITROQUINOLINE-1-OXIDE
4-HYDROXYAMINOQUINOLINE-1-OXIDE, CHROMOSOME ALTERATION, HAMSTER EMBRYONIC CELL (0098)
LUNG ADENOMA, ALUMINIUM (0096)
RAT LIVER CELL CULTURE, ULTRASTRUCTURE (0094)
SURFACTANT EFFECT, GASTRIC NEOPLASMS, RAT (0095)
YOSHIDA SARCOMA CELLS, CHROMOSOME ABERRATION, PERSISTENT NUCLEOLI (0097)

NITROSAZETIDINE
NITROSHEPTAMETHYLENEMINE, STOMACH, LUNG (0086)

N-NITROSOBUTYLUREA
LEUKEMOGENESIS (0001)
MAMMARY TUMOR, LEUKEMIA, MICE, RATS (0092)

NITROSOPIPERAZINE
CARCINOGENICITY, RATS (0087)

NITROSOTHOMOPHOLINE
CARCINOGENICITY, RATS (0087)

NITROSUREA
NERVOUS SYSTEM TUMORS, DESMOSTEROL, RAT (0089)

NOSE
NASAL SINUS, WOOD DUST, ADENOCARCINOMA (0113)

NUCLEIC ACID
BASIC PROTEIN ESTIMATION, MAMMARY ADENOCARCINOMA (0190)
BINDING, TUMOR INDUCTION, AFLATOXINS (0047)
SYNTHESIS, INHIBITION, AFLATOXIN (0049)
SYNTHESIS, LIVER REGENERATION, 7,12-DIMETHYLBENZ(A)ANTHRACENE (0050)

OCCUPATIONAL HAZARD
CANCER, 3,4-BENZOPYRENE, LARYNGEAL CANCER (0117)*
HEMATITE MINING, LUNG CANCER (0015)
OIL MIST EXPOSURE, NEOPLASM (0115)
SCROTAL CANCER, INDUSTRIAL HYGIENE (0116)

OIL
MIST EXPOSURE, NEOPLASM, OCCUPATIONAL HAZARD (0115)
MIST EXPOSURE, OCCUPATIONAL HAZARD, RESPIRATORY TRACT CANCER (0276)

ORAL CAVITY
RADIATION, VERROUS EPIDERMAL CARCINOMA ANAPLASTIC TRANSFORMATION, HUMAN (0131)

ORAL CONTRACEPTIVE
CERVICAL CANCER, CERVICAL DYSPLASIA (0281)

ORTHOAMINOAZOTOLUENE
LIVER, RIBOMYCIN, MOUSE (0025)

OSTEOSARCOMA
RADIUM POISONING, LYMPHOMYELOID CARCINOMA (0001)

PAGET'S DISEASE
X CHROMOSOME, SIMIAN VIRUS 40 (0245)

PAINT
PAINT REMOVERS, CARCINOMA, PENIS (0114)

INCREASE
 ISLET CELL TUMOR, PYRROLIZIDINE
 ALKALOID (0033)
 ANTOTHENIC ACID
 DEFICIENCY, FOCAL AVILLIOUS HYPERPLASIA
 MOUSE DUODENUM (0311)
 CYTIDINE
 FORESTOMACH, URETHAN, HAMSTER (0100)
 INFRARED EMISSION (0334)*
 CYTOLOGY
 SPONTANEOUS, LEUKEMIA, FISCHER, RAT
 (0323)
 CUTIS
 CARCINOMA, PAINT, PAINT REMOVERS
 (0114)
 ANTHRACENE
 K-REGION OXIDE, DIBENZ(A,H)ANTHRA-
 CENE, DNA, RNA (0047)
 PHOSPHOLIPID
 TURNOVER, NEOPLASTIC MAST CELL (0256)
 AGGLOMERATION
 LOW TEMPERATURE STORAGE, LYMPHOCYTE
 (0237)
 LYMPHOCYTE, CYCLIC AMP, TRANSFORMATION
 (0236)
 LYMPHOCYTE DIFFERENTIATION,
 DYNAMICS, MICROKINEMATOGRAPHY, MAN
 (0243)*
 LYMPHOCYTE TRANSFORMATION, LYMPHOMA,
 CELL CULTURE (0239)
 RIGID SATIVUM L., ERVUM LENS L.,
 LYMPHOBLASTIC TRANSFORMATION, IN
 VITRO, MAN (0242)*
 TRANSFORMATION, HUMAN LYMPHOCYTES,
 AFLATOXIN B (0045)
 CYTHERIA
 PHILADELPHIA CHROMOSOME, CHRONIC
 MYELOID LEUKEMIA (0010)
 TRANSFUSION, HYPOXIA, ERYTHROPOIETIN
 (0307)
 VERA, GRANULOCYTE, MURAMIDASE (0320)
 VPS
 JUVENILE, COLON, ALLERGY, FAMILIAL
 (0326)
 LYSACCHARIDE
 MUCOSUBSTANCES, CANINE MASTOCYTOMA
 (0329)
 CANCEROUS CONDITION
 SQUAMOUS CELL CARCINOMA, SUBMUCOUS
 FIBROSIS (0247)
 FENISOLONE
 MOLONEY LEUKEMIA VIRUS, LEUKEMIA,
 THYMUS (0173)
 MURINE LEUKEMIA VIRUS, THYMUS
 INDEPENDENT LYMPHOSARCOMA (0167)
 PREGNANCY
 BREAST CANCER, LACTATION (0321)
 HYDRAZINE, TOXICITY, RATS (0043)
 OLIFERATION
 CELLULAR, ISOPROTERENOL, CYTOPLASMIC
 RNA SYNTHESIS (0309)
 CONTROL, LYMPHOCYTE, RECOGNITION SITE
 (0008)
 KINETICS, CARCINOMA, 9,10-DIMETHYL-
 1,2-BENZANTHRACENE, IRRADIATION
 (0068)
 LYMPHOPROLIFERATIVE CHANGE, GERM-FREE
 MICE (0168)
 PROTEIN
 ALBUMIN SYNTHESIS, MORRIS HEPATOMA,
 TOTAL PROTEIN SYNTHESIS (0305)

BINDING, ORTHO-AMINOAZOTOLUENE,
 NUCLEIC ACID BINDING (0028)
 ALPHA-FETO-, AGE CORRELATION, LIVER
 (0231)
 ALPHA-FETO-, CARCINOEMBRYONIC ANTIGEN,
 GI CANCER (0240)*
 GLYCOPROTEIN, MAMMARY TUMOR AGENT,
 ANTIGEN (0191)
 GLYCOPROTEIN COMPONENT, ROUS SARCOMA
 VIRUS, AVIAN TUMOR VIRUS (0202)
 PARAPROTEIN, ELECTROPHORESIS, MULTIPLE
 MYELOMA (0333)*
 PARTICULATE THYROID PROTEINS, TUMOR
 (0255)
 PRINCIPAL PROTEIN CONJUGATES, CHEMICAL
 HEPATOCARCINOGENS (0050)
 RAT LIVER H, ANTI-H, 31-METHYLDIAZO-
 BENZENE (0053)
 PROPERTY
 GROWTH PEAK, BONE CANCER (0314)
 PYRROLIZIDINE ALKALOID
 PANCREATIC ISLET CELL TUMOR, AMBLYCKIA
 INTERMEDIA FISCH, HELIOTROPISM
 SUPRINUM (0033)
 4-QUINOLINE-1-OXIDE
 TERTIARY BUTYL HYDROPEROXIDE, FREE
 RADICAL, SQUAMOUS CELL CARCINOMA,
 MICE (0026)
 RADIATION
 CHRONIC, ECCRINE POROMA, THUMB (0134)
 GAMMA-IRRADIATION, MOUSE DUODENAL
 EPITHELIUM, CELL PRODUCTION (0123)
 HERATOMA, N,N'-2,7-FLUORENYLENERIS-
 ACETAMIDE, ACCELERATED INDUCTION
 (0040)
 IONIZING IRRADIATION, PULMONARY
 ISCHEMIA (0124)
 LYMPHOMA, INACTIVATION, IMMUNOLOGY,
 MOUSE (0223)
 ORAL CAVITY, VERRUCOUS EPIDERMAL
 CARCINOMA, ANAPLASTIC TRANSFORMATION
 HUMAN (0131)
 PHILADELPHIA CHROMOSOME, ACUTE
 LYMPHOCYTIC LEUKEMIA (0130)
 POSTIRRADIATION SARCOMA (0132)
 SARCOMA, SCAPULA, AXILLA, HUMAN (0133)
 SIMIAN VIRUS 40, MICE (0211)
 THERAPY, RADIATION-INDUCED THYROID
 NEOPLASMS, NODULAR GOITERS (0131)*
 ULTRAVIOLET IRRADIATION, MURINE SAR-
 COMA VIRUS INFECTION, CELL CYCLE
 (0198)
 WHOLE BODY IRRADIATION, LUNG ULTRA-
 STRUCTURE, ACID AND ALKALINE PHOS-
 PHATASE, GLYCINE INCORPORATION, RAT
 (0128)
 WHOLE BODY IRRADIATION, LUNG HISTO-
 CHEMISTRY, RAT (0127)
 WHOLE BODY IRRADIATION, SKIN LESIONS,
 HISTAMINE, BLOOD, RAT (0139)*
 X-IRRADIATION, MOUSE LEUKEMIA CELLS,
 ALLOGRAFT SURVIVAL (0225)
 X-IRRADIATION, MITOTIC DELAY,
 CHROMOSOMAL ABERRATION, CYSTEAMINE
 (0129)
 X-RAY THERAPY, STOMACH CANCER,
 FIBROSIS (0136)
 RADIOIODINE I31
 THYROID, FOLLICULAR ATROPHY, RAT
 (0125)
 RADIUM

* indicates a plain citation without accompanying abstract

POISONING, LYMPHOMYELOID CARCINOMA,
OSTEOSARCOMA (0001)

RESISTANCE
SV 40, GREEN MONKEY KIDNEY CELLS
(0214)

RETICULOENDOTHELIOSIS VIRUS
MARFAS DISEASE, PERIPHERAL NERVE
LESIONS (0161)

RHODAMINE
SARCOMA, GLUCOSE-6-PHOSPHATE
DEHYDROGENASE ISOZYMES, LIVER, RAT
(0035)

RNA
BENZ(A)PYRENE, IMMUNOREACTIVITY,
TRANSFER (0222)
CYTOPLASMIC SYNTHESIS, CELL PROLIFERA-
TION, ISOPROTERENOL (0309)
LIVER NUCLEAR, POLYMERASE, AFLATOXIN
B₁, RAT (0046)
METABOLISM, AMINE SYNTHESIS, THIO-
ACETAMIDE (0039)
METHYLATION, DIMETHYLNITROSAMINE,
S-ADENOSYL METHIONINE, RAT LIVER
(0082)
M-RNA, SENDAI VIRUS, HAMSTER, CHICK
EMBRYO (0207)
M-RNA SYNTHESIS, POLYOMA VIRUS,
MOUSE EMBRYO CELLS (0218)
RAUSCHER MURINE LEUKEMIA VIRUS,
NUCLEOCAPSID (0176)
TRANSCRIPTASE ACTIVITY, VIRUS, WOUND
TUMOR VIRUS (0148)
TRANSFER, HYPERMETHYLATION, DIMETHYL
SULFATE (0319)
TRANSFER, POLYOMA VIRUS, METHYLATION
(0217)
VIRAL RNA--DNA HYBRID MOLECULE,
DNA POLYMERASE TEMPLATE, SARCOMA-
LEUKEMIA (0143)

SALIVARY GLAND
MALIGNOMA, POLYMORPHIC ADENOMA,
EPIDEMIOLOGY, EASTERN GERMANY (0295)
MIXED TUMOR, HUMAN (0251)
NEOPLASM, ENVIRONMENT, VITAMIN A,
7,12-DIMETHYLBENZANTHRACENE, RAT
(0308)
TUMOR, POLYOMA VIRUS (0219)

SARCOMA
ANTIBODY, HUMAN, VIRUS (0147)
AVIAN LEUKOSIS, PATHOLOGY, MORPHOLOGY,
CELL PARTICLES (0324)
HERPES VIRUS HUMANIS, HAMSTER (0185)
K-237, SKIN-HETEROGENIZING VIRUS, MICE
(0144)
MCG1-SS, MCG1-AS, 20-METHYLCHOLAN-
THRENE, METASTASIS (0078)
METASTASIS, ROUS SARCOMA VIRUS,
MARMOSSET (0200)
ORNITHINE DECARBOXYLASE ACTIVITY
(0315)
RADIATION, SCAPULA, AXILLA, HUMAN
(0133)
RETICULAR CELL, EPIPHARYNGEAL CANCER,
EPITHELIAL CARCINOMA (0013)
RHODAMINE, GLUCOSE-6-PHOSPHATE
DEHYDROGENASE ISOZYMES, LIVER, RAT
(0035)
SOFT TISSUE, NEGRO, FIBROUS TISSUE
SARCOMA (0273)
TUMOR-SPECIFIC ANTIGEN, MURINE,
3-METHYLCHOLANTHRENE (0072)

WEIGHT, SEX, TEMPERATURE (0292)
X-RAY THERAPY, BREAST CANCER (0132)
YOSHIDA ASCITES, LUNG CARCINOMA,
METASTASIS PATTERN (0322)

SCAPULA
SARCOMA, AXILLA, RADIATION, HUMAN
(0133)

SCROTUM
CARCINOMA, OCCUPATIONAL FACTORS,
INDUSTRIAL HYGIENE (0116)

SEX
MORTALITY RATIO, LEUKEMIA, EPIDEMI-
OLOGY (0275)
TUMOR WEIGHT OF SARCOMA, TEMPERATURE
(0292)

SKIN
CANCER, CHRONIC LYMPHOCYTIC LEUKEMIA,
ETIOLOGY (0318)
CANCER, SOLAR KERATOSIS, EXPOSURE TO
SUNBURN (0269)
CERVIX, BREAST, IRAN, EPIDEMIOLOGY
(0284)
DIMETHYLBENZANTHRACENE, MELANOMA,
HAMSTER (0118)
ECCRINE POROMA, NOSE, RADIATION, TUMOR
(0134)
HETEROGENIZATION, GRAFT,
7,12-DIMETHYLBENZANTHRACENE
(0057)
HETEROGENIZING VIRUS, GENETIC TRAIT
(0145)
SQUAMOUS CELL CARCINOMA, TERTIARY
BUTYL HYDROPEROXIDE, 4-QUINOLINE-1-
OXIDE, MICE (0026)
SURGICAL LESIONS, HISTAMINE, WHOLE
BODY IRRADIATION, RAT (0139)
TUMOR SUSCEPTIBILITY, METHYLCHOL-
ANTHRENE, CIRCADIAN RHYTHM, MICE
(0074)
TUMORS, 3,3'-DIMETHYLBENZIDINE,
SERACEOUS GLAND, RAT (0023)

SOLID FUEL CONSUMPTION
CANCER DEATH RATE, IMPORT RATES FOR
COFFEE, TEA (0280)

SPLENOMEGALY
MURINE SARCOMA VIRUS, PLASMA VARIANT
(0196)
SHEEP ERYTHROCYTE IMMUNIZATION, VIRUS,
RAUSCHER LEUKEMIA VIRUS (0174)

STEROID
CONTRACEPTIVE, VAGINAL CYTOLOGY,
ESTRUS CYCLE (0120)
ESTRADIOL-17 BETA, LYMPHOID CELL
PROLIFERATION, ACUTE LYMPHOBLASTIC
LEUKEMIA, LYMPHOSARCOMA, MAN, IN
VITRO (0342)

STOMACH
ADENOCARCINOMA, SURFACTANT, 4-NITRO-
QUINOLINE-1-OXIDE, RAT (0095)
NITROSODAZETININE, NITROSODHEPTAMETHY-
L-CANCER, FIBROSIS, X-RAY THERAPY (0136)
FORESTOMACH PAPILLOMA, URETHAN (0100)
LENEIMINE, LUNG (0086)
ULCERS, CANCER, N-METHYL-N'-NITRO-N-
NITROGUANIDINE (0093)

STRESS
STOMACH ULCERS, CANCER, N-METHYL-N'-
NITRO-N-NITROGUANIDINE (0093)

SUNBURN
SOLAR KERATOSIS, SKIN CANCER (0269)

SURFACTANT

4-NITROQUINOLINE-1-OXIDE, STOMACH
ADENOCARCINOMA, RAT (0095)
SUSCEPTIBILITY
INHERITED, FRIEND LEUKEMIA VIRUS,
RESISTANT STRAIN (0149)
NEOPLASM, 7,12-DIMETHYLBENZ(A)ANTHRA-
CENE (0063)
SYNDROME
MEDICAL, MALIGNANCIES, SYMPTOM
ASSOCIATION (0011)
TURNER'S, EXTRAGONADAL TUMOR, NEURO-
BLASTOMA, GANGLIONEUROMA (0012)
TAR
CIGARETTE SMOKING, LUNG CANCER (0286)
TEMPERATURE
EFFECT, POLYHEDRAL CYTOPLASMIC
DEOXYRIBOVIRUS, VIRUS REPLICATION
(0189)
LOW, LYMPHOCYTE, HUMAN, PHYTO-
HEMAGGLUTININ (0237)
TERATOCARCINOGENESIS
GENITAL SLICE GRAFT, TEMPERATURE,
TESTES (0304)
TERATOMA
MOUSE EGG CYLINDER, EXTRAUTERINE
TRANSPLANTATION (0317)
TERTHYPHENYL
NEOPLASM, REACTOR COOLANT (0111)
TESTES
TERATOCARCINOGENESIS, GENITAL SLICE
GRAFT, TEMPERATURE (0304)
HIDACETAMIDE
RNA METABOLISM, AMINE SYNTHESIS (0039)
HISTOPAST
LYMPHOSARCOMA, CHROMOSOMAL ABERRA-
TIONS, MAN (0137)
THYMUS
EXTRACT, RESISTANCE TO TUMOR GROWTH,
MURINE SARCOMA VIRUS (0197)
THYMECTOMY, INFLUENCE OF MOUSE STRAIN,
MAMMARY TUMORIGENESIS (0192)
THYROID
MALIGNANT ADENOMA, X-RAY (0135)
PAPILLARY ADENOCARCINOMA, IODINE 131
(0124)
RADIATION-INDUCED NEOPLASMS, NODULAR
GOITERS, RADIATION THERAPY (0139)*
RAT, RADIOIODINE 131, FOLLICULAR
ATROPHY (0125)
TUMOR, RADIOACTIVE LABELING, PARTICU-
LATE THYROID PROTEINS (0255)
THYROIDITIS
CHRONIC, TRYPAN BLUE, RAT, AGE, SEX
(0034)
TOBACCO
CANCER DEATH RATE, SOLID FUEL CONSUMP-
TION, IMPORT RATES FOR COFFEE, TEA
(0280)
CIGARETTE SMOKING, BRONCHIAL
CARCINOMA, BEAGLE (0108)
CIGARETTE TAR, CARCINOMAS, LYMPHOMA,
NEWBORN ICR MICE (0105)
CILIOSTASIS, TECHNIQUE (0107)
CURSCHMANN SPIRAL, LUNG (0104)
LUNG CANCER, EPIDEMIOLOGY (0286)
LUNG CANCER, MORTALITY RATES (0017)
LUNG CANCER MORTALITY, TWIN PAIR
(0109)
SMOKING, 4-(4'-NITROBENZYL)PYRIDINE,
THIN LAYER CHROMATOGRAPHY (0106)

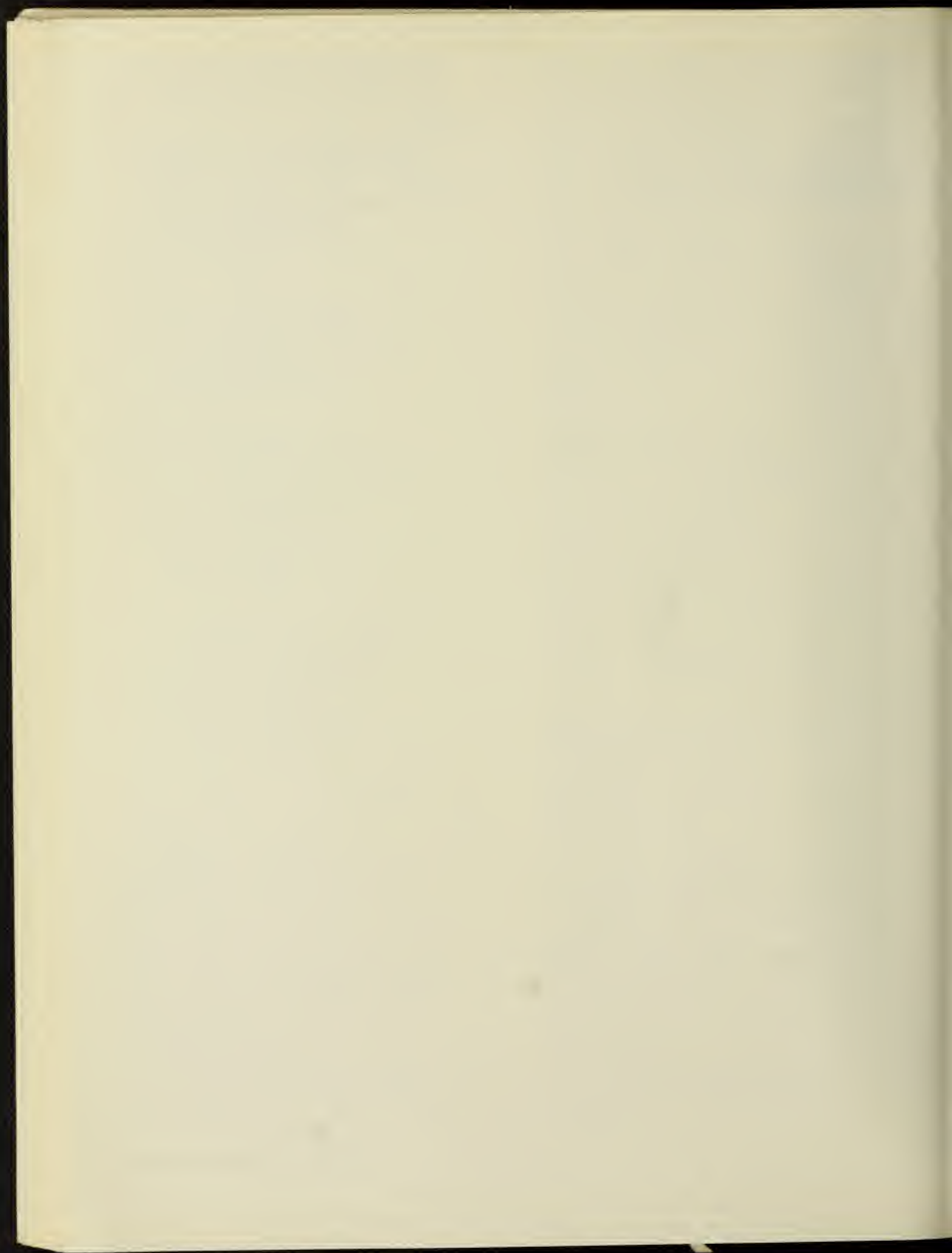
TRACHEA
CILIOSTASIS, EXPERIMENTAL TECHNIQUE,
TOBACCO SMOKE EXPOSURE (0107)
TRANSFORMATION
ADENOVIRUS, HAMSTER CELL LINE (0184)
ANO-RECTAL FISTULA, CARCINOMA, MAN
(0341)*
LEUKEMIA HELPER VIRUS, MURINE SARCOMA
VIRUS, AGAR SUSPENSION CULTURE
(0195)
MECHANISM, CROWN-GALL MODEL, DNA
(0243)*
VIRAL GENOME, TEMPERATURE SENSITIVE
MUTANT (0205)
TRANSPLANTATION
MOUSE EGG-CYLINDER, TERATOMA (0317)
TRANSPORT
SUGAR, ROUS SARCOMA VIRUS, CHICK
EMBRYO CELLS (0204)
TROPHOBLASTIC TUMOR
CHORIOEPITHELIOMA, IMMUNOLOGY,
PLATELET ANTIBODIES, LEUCOCYTE
ANTIBODIES (0227)
TRYPAN BLUE
CHRONIC THYROIDITIS, RAT, SEX, AGE
(0034)
DIMETHYLBENZANTHRACENE, HODGKIN'S
DISEASE, PATHOGENESIS (0019)*
TUMOR PROTECTION
7,12-DIMETHYLBENZ(A)ANTHRACENE,
GERM-FREE STATE (0065)
ULTRASTRUCTURE
CLASSIFICATION, HERPES SIMPLEX VIRUS
(0002)
CYTOLOGIC DIAGNOSIS, MAMMARY TUMOR,
ATYPIA, ASPIRATION BIOPSY (0242)*
LUNG, "HOLE BODY IRRADIATION, RAT
(0128)
LYMPHOBLAST, PHYTOHEMAGGLUTININ
INDUCED TRANSFORMATION, IN VITRO,
MAN (0242)*
RNA VIRUS, NUCLEOCAPSID (0176)
ROUS SARCOMA VIRUS, ROUS ASSOCIATED
VIRUS, VIRION CORE ANALYSIS (0206)
URETHAN
HAMSTER, FORESTOMACH PAPILLOMA (0100)
LUNG ADENOMA, RADIATION (0101)
MAMMARY GLAND TUMOR, SPLENECTOMY,
THYMECTOMY (0099)
UROGENITAL TUMOR
DNA POLYMERASE (0331)
UTERUS
BREAST, DOUBLE MALIGNANCY (0299)*
VAGINA
CYTOLOGY, ESTRUS CYCLE, STEROID
CONTRACEPTIVE (0120)*
VIRUS
ADENOVIRUS, CHICK EMBRYO CELLS,
INTERFERON INDUCTION (0178)
ADENOVIRUS, RABBIT HEART FIBROBLAST
CELL CULTURE, INFECTION VIRUS
FORMATION (0181)
ADENOVIRUS, TRANSFORMATION OF HAMSTER
CELL LINE (0184)
ADENOVIRUS, TUMOR SPECIFIC TRANS-
PLANTATION ANTIGEN, ADENOVIRUS
(0180)
ADENOVIRUS-ASSOCIATED VIRUSES, HUMAN
HERPES VIRUS (0179)
ADENOVIRUS TYPE 12, ANTIGEN, TUMOR,
FREEZING (0177)

* indicates a plain citation without accompanying abstract

AVIAN ADENOVIRUS, CHICKEN-EMBRYO-
 LETHAL-ORPHAN, FRENCHYMMOMAS (0182)
 AVIAN LEUKOSIS, EPIZOOTIC, CELL
 PARTICLES (0324)
 AVIAN LEUKOSIS-SARCOMA, VIRUS
 SUSCEPTIBILITY, ERYTHROCYTE ISOANTI-
 GEN (0160)
 AVIAN TUMOR, ROUS SARCOMA VIRUS,
 GLYCOPROTEIN COMPONENT (0202)
 BURKITT'S LYMPHOMA, MALARIA (0004)
 CHICKEN-EMBRYO-LETHAL-ORPHAN,
 ONCOGENICITY, HAMSTER (0208)
 DENSONNUCLEOSIS, ONCOGENICITY, DNA
 SYNTHESIS (0221)*
 EPSTEIN BARR, ANTIGENS, LYMPHOID CELLS
 (0154)
 EPSTEIN BARR, BURKITT LYMPHOMA, AUTO-
 IMMUNE SYSTEM, MALARIA (0005)
 EPSTEIN BARR, BURKITT LYMPHOMA SERUM
 ANTIBODY, NASOPHARYNGEAL CARCINOMA
 SERUM ANTIBODY (0153)
 EPSTEIN BARR, HERPES SIMPLEX, CYTO-
 MEGALOVIRUS, ANTIBODY, HODGKIN'S
 DISEASE (0155)
 EPSTEIN BARR, INFECTIOUS MONONUCLEO-
 SIS, BURKITT LYMPHOMA, LEUKEMIA
 (0004)
 EPSTEIN BARR, INFECTIOUS MONONUCLEO-
 SIS, BURKITT TUMOR (0154)
 EPSTEIN BARR, JUVENILE BURKITT
 LYMPHOMA, NECK, GERMANY (0152)
 FELINE LEUKEMIA, PURIFICATION,
 CONCENTRATION (0144)
 FELINE LEUKEMIA, VIRAL ANTIGEN,
 VIRAL ANTIBODY (0163)
 FRIEND, ANTIGENIC TUMOR CELLS, RAT
 (0170)
 FRIEND LEUKEMIA, INHERITED SUSCEPTI-
 BILITY, RESISTANT STRAIN (0169)
 GENITAL HERPES SIMPLEX, ANTIBODIES,
 HUMAN CERVIX CARCINOMA (0186)
 GROSS, THYMUS GRAFT, LEUKEMIA
 SUSCEPTIBILITY (0172)
 GROSS LEUKEMIA, LYMPHOID LEUKEMIA,
 AKP-A CULTURE, MOUSE (0171)
 HEMAGGLUTININATING ADENOVIRUS, HEMAG-
 GLUTINATION INHIBITOR, INTERACTION
 (0123)
 HERPES, GIANT CELL FORMATION, RABBIT
 KIDNEY, COMPOUND 48/80, INHIBITOR
 (0198)
 HERPES SIMPLEX, ULTRASTRUCTURE,
 CLASSIFICATION (0002)
 HERPES SIMPLEX, VIRUS-LIKE PARTICLES,
 LEUKEMIC BONE MARROW CELLS (0149)
 HERPES SIMPLEX TYPE-2, ENVIRONMENTAL
 FACTOR, CERVIX (0197)
 HERPES VIRUS HUMANIS, SARCOMA (0185)
 MAMMARY TUMOR, FOSTER-NURSED C3H/8 AND
 C3H/8 MICE, TRANSMISSION (0193)
 MAMMARY TUMOR, NODULE OUTGROWTH LINE O
 PARL/C, METHYLCOLANTHRENE (0076)
 MAMMARY TUMOR AGENT, ANTIGEN, GLYCO-
 PROTEIN (0191)
 MAREK'S DISEASE, HERPES, ANTIGEN,
 INFECTIVITY (0157)
 MAREK'S DISEASE, HERPES VIRUS CALI,
 PLAQUE TYPE, TISSUE CULTURE (0159)
 MOLONEY LEUKEMOGENIC, PREDNISOLONE,
 THYMUS (0173)
 MOUSE MAMMARY TUMOR, INOCULATION AGE,
 MILK ANTIGEN ASSAY (0194)
 MURINE LEUKEMIA, THYMUS-INDEPENDENT
 LYMPHOSARCOMA, PREDNISOLONE (0167)
 MURINE MYELOPROLIFERATIVE, LEUKEMIC
 MOUSE CELL CULTURE (0166)
 MURINE SARCOMA, BALB/3T3 CULTURE,
 MURINE LEUKEMIA VIRUS (0199)
 MURINE SARCOMA, CELL CYCLE, ULTRA-
 VIOLET IRRADIATION (0198)
 MURINE SARCOMA, LEUKEMIA HELPER VIRUS
 (0195)
 MURINE SARCOMA, PLASMA VARIANT,
 SPLENOMEGALY (0196)
 MURINE SARCOMA, THYMIC EXTRACT,
 RESISTANCE TO TUMOR GROWTH (0197)
 ONCOGENIC, DNA POLYMERASE, RNA HYBRID
 (0142)
 ONCOGENIC, DNA-DNA POLYMERASE DOUBLE
 STRAND TEMPLATE (0141)
 ONCOGENIC, ENDOGENOUS INTERFERON,
 REVIEW (0021)*
 ONCOGENIC, PRIMATE, LEUKEMIA, REVIEW
 (0003)
 ONCOGENIC RNA, CELL TRANSFORMATION,
 REVIEW (0020)*
 PARTICLE, ELECTRON MICROSCOPIC STUDY,
 MAMMARY CARCINOMA (0146)
 PARVOVIRUS 4-1, SV40, THYMIDINE
 KINASE, DNA SYNTHESIS (0210)
 POLYOMA, AT-TYPE FIBROSARCOMA, GC-TYPE
 ADENOCARCINOMA (0220)
 POLYOMA, BHK 21 HAMSTER ALL, DNA
 SYNTHESIS, SERUM (0214)
 POLYOMA, M-RNA SYNTHESIS, MOUSE
 EMBRYO CELLS (0218)
 POLYOMA, SALIVARY GLAND TUMOR (0219)
 POLYOMA, TRANSFER RNA, METHYLATION
 (0217)
 POLYOMA, TRANSFORMED CELL LINES,
 HAMSTER (0215)
 POLYOMA, U.V. IRRADIATION, TUMOR
 EXTRACT, IMMUNOTHERAPY, HAMSTER
 (0241)*
 RAUSCHER LEUKEMIA, SPLENOMEGALY, SHEEP
 ERYTHROCYTE IMMUNIZATION (0174)
 RAUSCHER MURINE LEUKEMIA, ULTRA-
 STRUCTURE, DNA (0174)
 ROUS SARCOMA, CHICK EMBRYO CELLS,
 SUGAR TRANSPORT (0204)
 ROUS SARCOMA, DNA ISOLATION (0203)
 ROUS SARCOMA, METASTASIS, NEOPLASM,
 MAMMOSET (0200)
 ROUS SARCOMA, ROUS ASSOCIATED, VIRION
 COPE ANALYSIS (0206)
 ROUS SARCOMA, TRANSFORMED STATE,
 TEMPERATURE SENSITIVE MUTANT (0205)
 ROUS SARCOMA VIRUS COAT ANTIGEN,
 HETEROKARYOTIC CELLS, VIRULENT CELL
 FUSION (0201)
 SARCOMA, ANTIBODY, HUMAN (0147)
 SARCOMA-LEUKEMIA VIRUS, VIRAL RNA-DNA
 HYBRID MOLECULE, DNA POLYMERASE
 TEMPLATE (0143)
 SENDAI, HAMSTER, CHICK EMBRYO, M-RNA
 (0207)
 SKIN-HETEROGENIZING, SARCOMA K-237,
 MICE (0144)
 SKIN HETEROGENIZING, STRAIN SPECIFIC
 VIRUS, GENETIC TRAIT (0145)
 SV40, ANTIBODY, PREGNANT HAMSTERS
 (0213)

SV40, GREEN MONKEY KIDNEY CELLS,
RESISTANCE (0214)
SV40, HUMAN, HAMSTER, KINETICS (0209)
SV40, PAGET'S DISEASE, X CHROMOSOME
(0245)
SV40, SURFACE AND TUMOR ANTIGENS,
VIRUS-SPECIFIED DNA (0209)
SV40 TRANSFORMED, MOUSE CELL, SURFACE
COMPONENT (0212)
SV40, X-RAY IRRADIATION, MICE (0211)
TEMPERATURE, POLYHEDRAL CYTOPLASMIC

DEOXYRICOVIRUS, REPLICATION (0189)
TYPE C PARTICLE, EMBRYONIC CULTURE,
RAUSCHER MURINE LEUKEMIA (0175)
WOUND TUMOR, RNA TRANSCRIPTASE
ACTIVITY (0148)
VITAMIN A
DEFICIENCY, SALIVARY GLAND NEOPLASM,
7,12-DIMETHYLBENZANTHRACENE, RAT
(0308)
WOOD DUST
ADENOCARCINOMA, NASAL SYSTEM (0113)



U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

OFFICIAL BUSINESS

PENALTY FOR PRIVATE USE, \$300

If you do not desire to continue receiving this publication, please CHECK HERE ☐;
tear off this label and return it to the above address. Your name will then be
promptly removed from the appropriate mailing list.

425
P

Vet
Med

SEPTEMBER-OCTOBER 1970

Abstract Nos. 344-830

Vol. 9
No. 3-4

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health



CARCINOGENESIS ABSTRACTS

A monthly publication of the

National Cancer Institute

Editor

Robert Love, M.D.
Jefferson Medical College, Philadelphia

Associate Editor

George P. Studzinski, M.D.
Jefferson Medical College, Philadelphia

NCI Staff Consultants

Gerald L. Bartlett, M.D.
Louis P. Greenberg, M.S.
Howard R. Rosenberg, M.S.
Elizabeth Weisberger, Ph.D.

Literature Selected, Abstracted, and Indexed
by

The Franklin Institute Research Laboratories
Science Information Services
Biomedical Section

M. H. Fukami, Ph.D., Technical Editor

Contract Number NIH-71-2073

Public Health Service, USDHEW

THE LIBRARY OF THE
JUL 14 1971
UNIVERSITY OF ILLINOIS



PREFACE

Carcinogenesis Abstracts is a publication of the National Cancer Institute. The journal serves as a vehicle through which current documentation of carcinogenesis research highlights are compiled, condensed, and disseminated on a regular basis. It represents an integral part of the Institute's program of fostering and supporting coordinated research into cancer etiology. Issues of *Carcinogenesis Abstracts* normally contain two-hundred abstracts and twenty citations (unaccompanied by corresponding abstracts). Abstracts and citations refer to the current scientific literature that describes the most significant carcinogenesis research carried on at the National Cancer Institute, other governmental agencies, and private institutions. *Carcinogenesis Abstracts* is intended to be a highly useful current awareness tool for scientists engaged in carcinogenesis research or related areas. The great number and diversity of publications relevant to carcinogenesis make imperative the availability of this service to investigators whose work requires that they keep abreast with current developments in the field.

Carcinogenesis Abstracts is normally published monthly. Volume IX covers the scientific literature published from July 1970 through June 1971. A cumulative subject and author index for Volume IX will be published shortly after the final regular issue. This journal is available free of charge to libraries and to individuals who have a professional interest in carcinogenesis. Requests for *Carcinogenesis Abstracts* from qualified individuals should include statements of their relationship to carcinogenesis research. All correspondence should be addressed as follows:

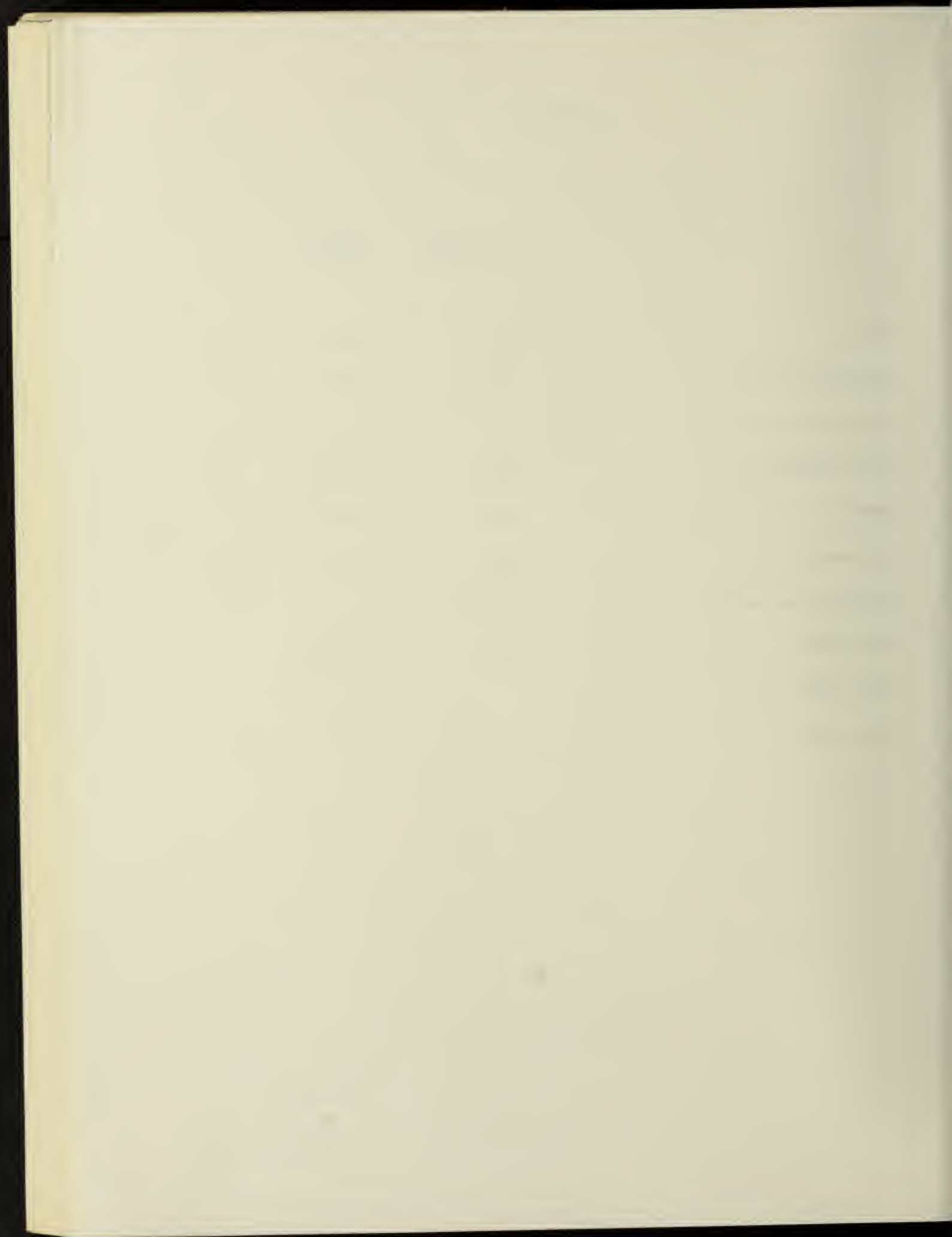
Carcinogenesis Abstracts
Etiology Area
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20014

Use of funds for printing this publication
approved by the Director of the Bureau of
the Budget on July 25, 1967.



CONTENTS

	Cross Reference Abbreviations	Abstracts, Citations	Page
REVIEW	(Rev).	0344-0393	67
CHEMICAL CARCINOGENESIS.	(Chem)	0394-0520	76
PHYSICAL CARCINOGENESIS.	(Phys)	0521-0549	104
VIRAL CARCINOGENESIS	(Viral).	0550-0690	111
IMMUNOLOGY	(Immun).	0691-0734	143
PATHOGENESIS	(Path)	0735-0749	152
EPIDEMIOLOGY AND BIOMETRY.	(Epid-Biom).	0750-0768	155
MISCELLANEOUS.	(Misc)	0769-0830	159
AUTHOR INDEX			i
SUBJECT INDEX			xii



NOTE

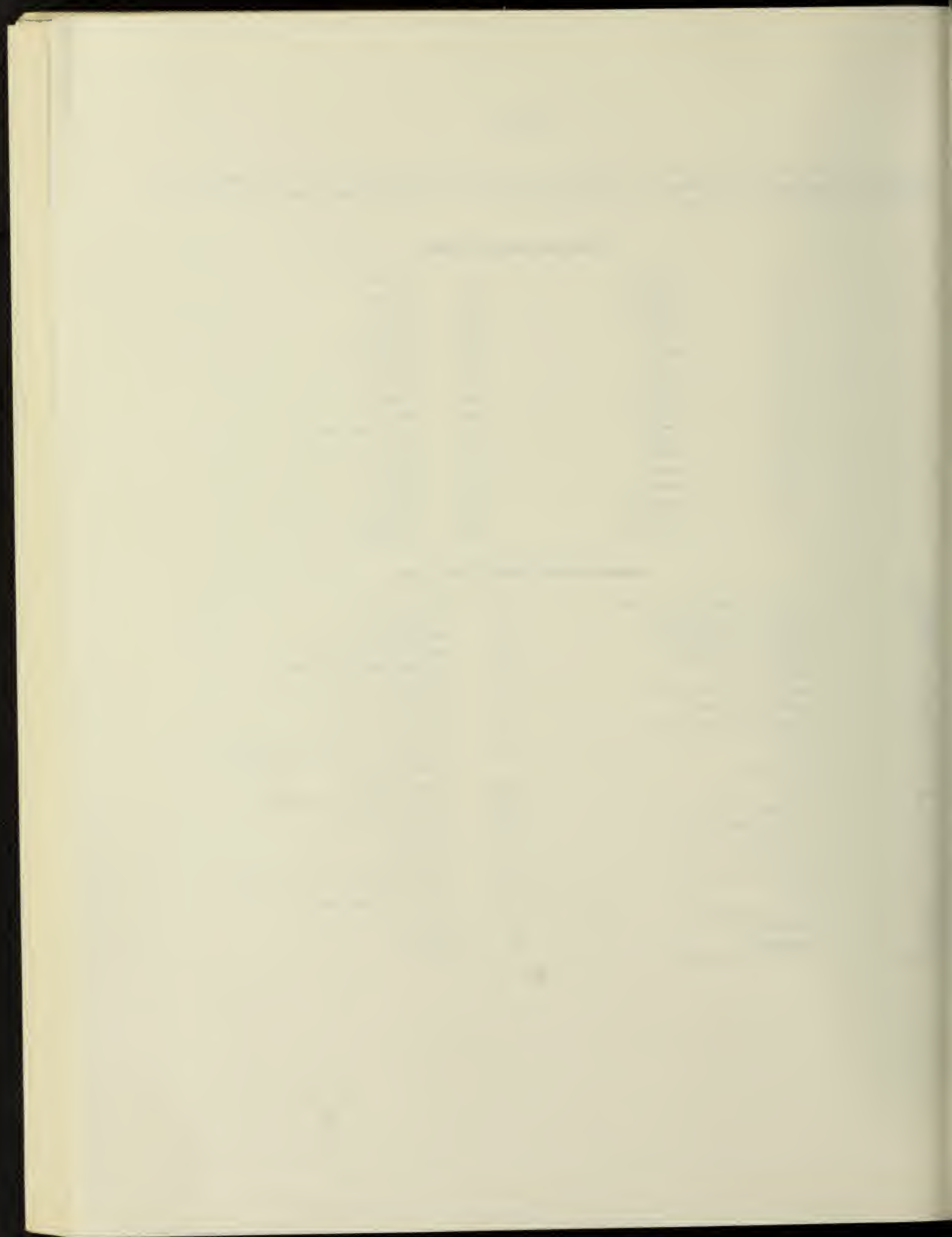
Journal names are abbreviated according to the list of abbreviations used by *Index Medicus*. For journals not covered by *Index Medicus*, the abbreviations (with some modifications) found in *World Medical Periodicals*, 3rd Edition, are used.

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	It.	Italian
Ar.	Arabic	Jap.	Japanese
Bul.	Bulgarian	Kor.	Korean
Ch.	Chinese	Latv.	Latvian
Cz.	Czech	Lith.	Lithuanian
Dan.	Danish	Nor.	Norwegian
Dut.	Dutch	Pol.	Polish
E.	English	Por.	Portuguese
Eston.	Estonian	Rum.	Rumanian
Fin.	Finnish	Rus.	Russian
Fl.	Flemish	Ser.	Serbo-Croatian
Fr.	French	Sl.	Slovak
Ger.	German	Sp.	Spanish
Gr.	Greek	Sw.	Swedish
Heb.	Hebrew	Th.	Thai
Hun.	Hungarian	Turk.	Turkish
Ic.	Icelandic	Uk.	Ukrainian
ln.	Indonesian	Viet.	Vietnamese

ABBREVIATIONS USED IN ABSTRACTS

ACTH	adrenocorticotrophic hormone	mg	milligram(s)
ADP	adenosine diphosphate	min	minute(s)
AMP	adenosine monophosphate	ml	milliliter(s)
ATP	adenosine triphosphate	mm	millimeter(s)
C	degrees centigrade	MTD	maximum tolerated dose
cm	centimeter(s)	ng	nanogram (10^{-9})
CNS	central nervous system	pg	picogram (10^{-12})
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	ppm	parts per million
e.g.	for example	r	Roentgen
g	gram(s)	RBC	red blood cells (erythrocytes), red blood count
µg	microgram(s)	resp.	respectively
hr	hour(s)	Rev.	review (only in citations)
i.m.	intramuscular	RNA	ribonucleic acid
i.p.	intraperitoneal	s.c.	subcutaneous
IU	international unit(s)	sec	second(s)
i.v.	intravenous	U	unit(s)
kg	kilogram(s)	UV	ultraviolet
LD ₅₀	median lethal dose(s)	WBC	white blood cells (leukocytes), white blood count
m	meter(s)	wk	week
M	molar	wt	weight
mEq	milliequivalent(s)	yr	year(s)
mM	millimolar		
µM	micromolar		
mC, µC	milli-,microcurie(s)		



0348-0352)

- 0344 THE FUTURE OF CYTOGENETICS. (E.) De Grouchy, J. (Hosp. Child. Dis., Paris, France). *Rev Europ Etud Clin Biol* 15(7):727-728, 1970.

Recent advances in cytogenetics, including the discovery of chromosomal abnormalities associated with overt pathology, have raised the question of the mechanism relating chromosomal imbalance and the corresponding embryonic disorder. In the area of carcinogenesis, the central question is whether the chromosomal abnormalities observed in malignant cells are the cause or the consequence of carcinogenesis. The discovery of an association between the Philadelphia chromosome and leukemia may indicate that there exists a causal relationship between aberrations and neoplastic development. Chromosomal changes in neoplastic cells are apparently not static but evolving, and this clonal evolution may in the case of some malignant conditions (chronic myeloid leukemia) be associated with the clinical development of the condition. New techniques available to the cytogeneticist such as human cell fertilization *in vitro*, *in utero* studies, cell culture and hybridization can be expected to shed much light on these issues. (6 references)

- 0345 AN OPTICAL-RESIDUE SINGLET-OXYGEN THEORY OF PHOTOCARCINOGENICITY. (E.) Khan, A. U. (Inst. Molec. Biophys., Florida State U., Tallahassee) and M. Kasha. *Ann NY Acad Sci* 171(1):24-33, 1970.

A theory of photocarcinogenicity is presented in which the 2 active sites for electrophilic addition, K (adjacent carbon atoms) and L (addition in *para*-positions across the ring), determine only the initial binding of the polycyclic hydrocarbon to the cell constituents. The carcinogenic potency of the molecule is dependent on the generation of singlet molecular oxygen after optical excitation of the optical residue aromatic hydrocarbon. The proposed optical-residue model demands that the residual molecule of a carcinogenic polycyclic hydrocarbon continue to absorb natural sunlight after binding to a cell constituent, that it have a reasonable rate for inter-system-crossing from the singlet excited state to the triplet state, and that the energetic disposition of its electronic states be favorable for singlet oxygen photosensitization. A definite photic effect on benzo[a]pyrene carcinogenesis was noted when painted mice housed in a special darkroom developed 50% fewer gross skin tumors than mice housed in a normally lighted room. Further studies are necessary to determine wavelength dependence, the molecular damage site, and the subcellular biochemical mechanisms involved. (42 references)

- 0346 CELL-CARCINOGEN INTERACTION *IN VITRO*. (E.) Diamond, L. (Wistar Inst. Anat. Biol., Philadelphia, Pa.). *Trans NY Acad Sci* 32(2):234-241, 1970.

Several studies have been conducted to explain the differences in sensitivity to carcinogenic hydrocarbon-induced cytotoxicity evinced by various cell

systems, and several parameters of carcinogen interaction with a variety of cells have been examined. Autoradiographic and fluorescence microscopic studies have shown that resistance to cytotoxicity is not due to the failure of cells to take up the hydrocarbons. However, it has been shown that in cells grown with tritium-labeled 7,12-dimethylbenz(a)anthracene, cytotoxicity-sensitive cells were able to bind 5-50 times more label than were resistant cells; a similar correlation between binding and cytotoxicity was found for 3,4-benzopyrene. Binding of hydrocarbons to cellular macromolecules has been shown to be mediated by microsomal hydroxylase; furthermore, microsomal hydroxylase inhibits hydrocarbon binding in hamster embryo cells pretreated with α -naphthoflavone. α -Naphthoflavone also prevented the inhibition of cell multiplication normally induced by either 3,4-benzopyrene or 7,12-dimethylbenz(a)anthracene. Three parameters of cell-carcinogen interaction in monolayer cultures can be correlated with sensitivity of cells to the induced cytotoxic effect: the presence and inducibility of the microsomal aryl hydroxylase enzyme complex; the metabolism of the hydrocarbon to derivatives which are more water-soluble than the original hydrocarbon; and the binding of the hydrocarbon or its derivatives to cellular macromolecules. In cells resistant to carcinogen-induced cytotoxicity, these activities are absent or reduced, indicating that metabolism of the hydrocarbon is essential for its toxic effect on the cell. Metabolism and binding of a hydrocarbon may also be essential for its carcinogenic effect on cells; experiments to test this hypothesis by determining the efficiency of carcinogen-induced transformation in the presence of α -naphthoflavone are now in progress. Transformation in the presence of α -naphthoflavone of cells normally sensitive to the cytotoxic effect of the carcinogen would suggest that cytotoxicity and transformation are different processes. (29 references)

- 0347 CARCINOGENIC PROPERTIES, STRUCTURE AND REACTIVITY OF PHENOLS. (Rus.) Gubergits, M. Ya. (Chem. Inst. Acad. Sci. ESSR, USSR) and U. E. Kirso. *Vop Onkol* 16(8):96-100, 1970.

The carcinogenic, promoting, toxic and inhibitory effects of phenolic compounds are reviewed in an attempt to establish a quantitative structure-activity relationship. Carcinogenicity is increased by alkyl and halogen substituents which induce an increase of electron density around the -OH group; carcinogenicity is decreased by substituents like -CHO, -COOH and -NO₂ which have the opposite effect. The quantitative correlation between the increase of electron density around the reactive group and the decrease of carcinogenic and promoting activity of phenol compounds is expressed by a modified Hammett-Taft equation. The carcinogenicity of a phenolic compound appears to be related to its nucleophilicity; toxicity and carcinogenicity are negatively correlated, and the toxicity and inhibitory (antioxidant) effects are probably related to the electrophilic properties of the compound. (35 references)

REVIEW

- 0348 TRYPTOPHAN-CARCINOGEN-RESONANCE HYDROPHOBIC PROTEIN BINDING AND CHEMICAL CARCINOGENESIS. (Ger.) Franke, R. (Inst. Physiol. Biol. Chem., Humboldt U., Berlin, Germany). *Arch Geschwulstforsch* 36(1):30-33, 1970.

The Birks theory that there is a correlation between carcinogenic activity and the tryptophan overlap integral (J_1), subject to the formation of protein complexes by the hydrocarbons is considered. This theory has been criticized on the grounds of quantum mechanics, but without taking into account complex formation with proteins. A suitable dimension for the characterization of complex formation between protein and carbohydrate is, as shown previously, the logarithm of the binding constant for the binding of carbohydrate to human serum protein, $\log K_B$. A rank correlation statistical analysis was carried out to find the correlation between J_1 and carcinogenic activity by means of the protein binding and thus to reevaluate the Birks theory. The results proved that the correlation between carcinogenic activity and overlap integrals had no real physical significance. (9 references)

- 0349 SUSCEPTIBILITY TO TRANSFORMATION. (E.) Anonymous *Nature* 228(5276):1032, 1970.

Experiments have been designed to investigate the possibility that persons whose cells are especially susceptible to *in vitro* transformation by SV40 are persons at a high risk of developing cancer. Studies have shown that human cells which are differentially susceptible to infection by SV40 particles are equally susceptible to infection by SV40 DNA alone, a result suggesting that relative resistance or susceptibility to SV40 infection depends on a block or the lack of a block to an early event in infection. This hypothesis is further supported by the finding that, in cells infected with SV40 DNA, all cells have similar tumor-antigen contents and similar rates of transformation, while in cells infected with virus alone, cells having the highest tumor-antigen contents are the cells with the highest rate of transformation. Other experiments further suggest that transformation of infected cells and the production of tumor-antigen are closely related processes. (2 references)

- 0350 NEW GROWTH AND VIRUSES. (E.) Stoker, M. (Imperial Cancer Res. Fund Lab., London, England). *Brit Med J* 3(5722):541-545, 1970.

Characteristics of growth regulation were studied in individual normal cells (3T3 mouse cell line and BHK21 hamster cell line) and compared with those in polyoma-transformed cells. A high cell density causes normal cells to stop growing in the G_1 phase unless the density is reduced; preventing cells from anchorage to a rigid surface stops growth. Protein associated with the gammaglobulin fraction of serum is a requirement for growth although this factor (or factors) is not species specific in its effect. Addition of fresh serum to resting confluent cultures of 3T3 cells causes further growth, but the

probability that a particular cell will respond depends on its topography (position in relation to other cells) so that a free cell in a wounded area may be 8 times more sensitive to serum than a cell in an undisturbed sheet. Transformed cells are less sensitive to density-dependent inhibition and continue to grow in thick layers freely in suspension without contact to a rigid surface. The transformed cells can continue one or two mitotic divisions in serum levels inhibitory for normal cells, while DNA synthesis continues until the cells degenerate without undergoing mitosis. (30 references)

- 0351 VIRAL ETIOLOGY OF CANCER, LEUKEMIA AND ALLIED DISEASES. (E.) Gross, L. (VA Hosp., Bronx, N.Y.). *CA* 20(4):243-247, 1970.

Experimental observations supporting the hypothesis that latent oncogenic virus are present in many normal and healthy hosts and can be activated by a "oncogenic situation" are reviewed. Studies have shown that oncogenic viruses (e.g., Rous chicken sarcoma virus) found originally in one species may be pathogenic for other species, and that certain viruses which are latent in one species may be oncogenic for other species (e.g., SV40 which is latent in the rhesus monkey causes sarcomata in hamsters). In instances of radiation-induced leukemia in mice, the leukemic tissues of these mice were found to harbor a filterable leukemogenic virus. In addition, leukemia and lymphoma viruses found in leukemic mice, produce leukemia in other mice and in rats when transferred from the original host. These latent oncogenic viruses which may be normally present in large numbers of individual animals and humans become pathogenic only when activated by some trigger such as irradiation, chemical carcinogens, or metabolic or hormonal factors. The presence of an inactive but potentially oncogenic virus in healthy humans might be indicated by the individual's family record; those with family histories of carcinoma or leukemia may harbor inactive viruses. (60 references)

- 0352 FOOTPRINTS OF HUMAN CANCER VIRUSES? (E.) Anonymous. *Nature* 228(5275):907-908, 1970.

The discovery that human leukemic cells harbor reverse transcriptases which use RNA as the template for DNA synthesis can be interpreted as evidence that at least some human cancers have a viral etiology. Experiments by Gallo, Yang, *et al* have shown that antibodies against group specific antigens of murine sarcoma virus inactivate the reverse transcriptase in murine sarcoma virus and other viruses; should these antibodies also inactivate human leukemia polymerase activities, strong evidence would be provided that human leukemia viruses do exist. The only trace of such human viruses may be these reverse transcriptases. Related experiments by Pollack *et al* have suggested that an increase in number of chromosomes in some cells accompanies a loss of several of the characteristics of the malignant transformed condition. These results may indicate that relapses in symptoms of malignancy fol-

(0353-0356)

lowing an initial improvement occur because hyperploid cells give rise to cells with low chromosome numbers which are especially susceptible to malignant transformation. (no references)

0353 INFECTIOUS MONONUCLEOSIS: RECENT DEVELOPMENTS. (E.) Banatvala, J. E. (St. Thomas' Hosp. Med. Sch., London, England). *Brit J Haemat* 19(2):129-133, 1970.

Evidence for a causal association between Epstein-Barr virus and infectious mononucleosis is not conclusive, despite the fact that the virus is a commonly encountered infectious agent which is associated with Burkitt's lymphoma. One study has shown that only those members of the study group whose sera were negative for Epstein-Barr virus antibodies developed infectious mononucleosis. Furthermore, following the onset of illness, titers of virus antibodies rose significantly to 40-640. Epstein-Barr virus antibodies are of global distribution, and their presence is correlated with factors such as age and socio-economic status. Young children have been found to be antibody seropositive in 50-80% of test populations; those of low socio-economic status are more often positive than those of other levels. Evidence that Epstein-Barr virus causes infectious mononucleosis is provided by the fact that antibodies to the virus appear to protect against infectious mononucleosis. Moreover, almost all patients with infectious mononucleosis develop high or rising titers of Epstein-Barr antibodies during the course of their illness. The virus has been shown to replicate only in the cells of the lymphoreticular system and to stimulate leukocytes of patients with infectious mononucleosis to proliferate into blastoid cell cultures which harbor Epstein-Barr virus. (20 references)

0354 IMMUNOLOGICAL DISORDERS IN THE ETIOLOGY OF LYMPHORETICULAR NEOPLASMS. (E.) Hoerni, B. (Bergonie Found., Bordeaux, France) and G. Laporte. *Europ J Clin Biol Res* 15(8):841-850, 1970.

Data implicating immunological factors in the development of lymphoreticular neoplasms and suggested mechanisms for the immunological initiation of growth are reviewed. Congenital or acquired (thymectomy, chemical carcinogens, or immunosuppressive drugs) immune deficiencies as well as immunoproliferative disorders apparently increase the frequency of malignant lymphomas in animals. An autoimmune disease found in NZB/B1 mice and minks preceded the development of lymphoma, while spleen cell grafting and repeated mineral oil (or antigen) injections led to malignant lymphoid tumors. Similar findings in man showed that immunological deficiencies (agammaglobulinemia) and lymphoproliferative disorders (systemic lupus erythematosus) resulted in increased incidence of lymphomas. Viruses may become infectious in an immunologically deficient environment, and repeated infections produce an increased proliferation of lymphoreticular cells with higher risks for neoplastic mutation. If a neoplastic clone undergoes proliferation, the antibodies produced against the transformed cells

(7S antibodies) may actually be enhancing antibodies, and certain viruses may produce transformed cells or neoantigens which are histochemically similar to the host cells, resulting in cancerous proliferation even with normal defenses. Evidence for the importance of immunological factors in carcinogenesis is increasing. (124 references)

0355 THE CONCEPT OF IMMUNOLOGICAL SURVEILLANCE. (E.) Burnet, F. M. (U. Melbourne, Parkville, Victoria, Australia). *Progr Exp Tumor Res* 13:1-27, 1970.

The concept of immunological surveillance (the immunological mechanism present in large long-lived animals for eliminating or inactivating the potentially dangerous mutant cell produced through inheritable genetic changes which must be common in somatic cells) was examined. Implications of such a concept are that the incidence of malignancies initiated during immunity deficiency will be high, that pathological conditions associated with depression of the thymus-dependent immune system should be associated with increased likelihood of neoplasia, that late activity of the immune system might occasionally cause spontaneous regression of tumors, and that more histologically observable foci of cancer than could ever develop to definite tumors should be observed at autopsy of cancerous organs. Representative studies that have been conducted on the effects of immunosuppressive agents, neonatal thymectomy, fetal or perinatal tolerance, immune paralysis, and specific resistance to tumor implantation suggest that the concept of surveillance is valid. The hypothesis for the evolution of adaptive immunity (responses to the development of parasitism by early cyclostomes on hosts of similar character) and a similar modification of genetic control leading to the appearance of cancer may substantiate the evolutionary principle that the new mechanism of immunity was further refined for use against the new danger. (82 references)

0356 CONTROL OF NEOPLASIA BY IMMUNOLOGICAL MEANS: AN ASSESSMENT OF A NEW APPROACH. (E.) Plescia, O. J. (Inst. Microbiol., Rutgers U., New Brunswick, N. J.) and W. Braun. *G Batt Virolog Immun* 63(1-6):7-18, 1970.

Attempts have been made, based on theoretical considerations concerning host receptivity for a tumor, to develop a method for the preparation of effective tumor vaccines. Theoretically, a host may fail to reject a syngenic tumor possessing tumor-specific transplantation antigen for any of the following reasons: the tumor is not sufficiently foreign antigenically to elicit an adequate immune response; the tumor is not subject to biological control and therefore can develop beyond the control of a normal immune response; because of its location, the tumor may elicit a humoral, rather than cell-mediated response; the host may become specifically tolerant to the tumor or generally unresponsive as a result of immunosuppression caused

by oncogens or by the aging process. Experimental results in the development of a tumor vaccine based on this analysis have attempted to make tumor tissue more foreign antigenically by conjugating it to a "carrier" such as agents of the dinitrophenyl group or methylated bovine serum albumin. Tumors treated in this way, implanted s.c. in hosts, are effective as a vaccine and promote rejection of challenge tumor cells. The vaccine efficacy increased when an adjuvant was used to enhance the host response. Although such vaccines have proved effective prophylactically and therapeutically, a dearth of knowledge concerning the etiology of spontaneous tumors and tumor-specific transplantation antigens renders tumor vaccines feasible only as adjunct therapy following surgery as a means of controlling residual tumor tissue development. (29 references)

- 0357 IMMUNOSUPPRESSION AND NEOPLASIA. (E.) Balner, H. (Radiobiol. Inst. TNO, Rijswijk, Z.H., Netherlands). *Europ J Clin Biol Res* 15(6):599-604, 1970.

Prolonged immune deficiency has been shown experimentally to be a factor which contributes to susceptibility to oncogenic viruses and to carcinogens that induce tumors with a rather high tumor-specific antigenicity. In most experiments the immune-deficient state was achieved by conventional immunosuppressive agents (Imuran and steroids, whole body irradiation, alkylating agents, antimetabolites), early thymectomy or treatment with anti-lymphocyte serum. More recently, it was also reported that the tumor incidence in transplant patients under chronic immunosuppressive treatment is significantly higher than in comparable control individuals. No evidence was found that the role of anti-lymphocyte serum in the breakdown of a hypothetical surveillance mechanism against neoplasia was different from that of conventional immunosuppressive agents. Immunosuppression seems to enhance the susceptibility to oncogenic factors in animals by interfering with cellular defences. (39 references)

- 0358 THE ROLE OF IMMUNOLOGY IN HUMAN CANCER RESEARCH. (E.) Gold, P. (Montreal Gen. Hosp., Quebec, Canada). *Canad Med Ass J* 103(10):1043-1051, 1970.

Ethical limitations on human experimentation and wide genetic diversity of the population have made research of human cancers difficult, but the evidence of tumor-specific transplantation antigens in a wide variety of experimental tumors in animals and modern technology have resulted in the detection of tumor-specific antigenicity in some human tumor systems. The carcinoembryonic antigen of the human digestive system and α -fetoprotein in hepatomas as well as characteristic immune reactions observed with sera of patients with Burkitt's lymphoma, malignant melanoma, osteosarcoma and neuroblastoma are examples of recent cancer immunology research. Some of these systems apparently stimulate an immunologic response by the cancer patient, suggesting that where cancer growth has developed the defense mechanism has been over-

whelmed or is defective. Application of the tumor-specific antigenicity to cancer diagnosis has been encouraging and immunotherapy for cancer patients is being investigated. (83 references)

- 0359 A REAPPRAISAL OF THE "MYELOPROLIFERATIVE DISEASE" CONCEPT. (E.) Gilbert, H. S. (Mount Sinai Sch. Med., City U., New York, N. Y.) *Mount Sinai J Med* 37(4):426-435, 1970.

The trend toward subsuming such disorders as polycythemia vera, agnogenic myeloid metaplasia, essential thrombocythemia, erythroleukemia, and chronic myelocytic leukemia under the single rubric of "myeloproliferative disorders" is a relatively recent one and has supplanted an earlier tendency to regard each of these conditions as a separate disease entity. The rationale for unifying these various diseases in a single category was the existence of a hypothetical precursor cell with the potential for developing into cells of the erythroid, myeloid or megakaryocytic series. Recent (1961) it has been shown that such a pluripotential stem cell does in fact exist, and the development of techniques for karyotyping cells have supported the hypothesis that there is a common ancestor cell for erythroid and granulocyte cells by showing that the abnormal Philadelphia chromosome is present in both erythroid and myeloid precursor cells. However, both genetic and biochemical studies have recently cast doubt on the feasibility of regarding all the "myeloproliferative diseases" as members of 1 nosologic family. The continuing failure to demonstrate the Philadelphia chromosome in polycythemia vera during its various stages, the differences in levels and behavior of leucocyte alkaline phosphatase activity in all myeloproliferative conditions, and the failure to observe transitions in the karyotype or enzyme picture despite apparent clinical transition from polycythemia vera to a picture resembling chronic myelocytic leukemia, tend to polarize at least 2 the members of the myeloproliferative syndromes chronic myelocytic leukemia being set apart from polycythemia vera. The remaining entities included in the group would appear to segregate with polycythemia vera on the basis of current knowledge. (34 references)

- 0360 THYMIC TUMORS, ASSOCIATED GENERAL SYNDROMES AND CARCINOGENESIS. (Fr.) Saeges F. (Fac. Med. Lausanne, Switzerland) and G. Zoupas. *Entretiens Bichat* 49-56, 1970.

Recent clinical and experimental data indicate that patients subjected to organ transplants become susceptible to malignancy of the immunopoietic system. The frequent coexistence of thymoma and general immunological disorders such as myasthenia gravis, aplastic anemia, acquired hypogammaglobulinemia, collagenoses and autoimmune diseases indicate that the thymus is a key organ in both the development and maintenance of the immunological potential of the organism. A high incidence of lympho-epithelial thymoma is predicted for long-surviving patients with organ transplants. (no references)

0361 TUMOR SPECIFIC ANTIGENS ASSOCIATED WITH CHEMICALLY INDUCED TUMORS. (E.) Baldwin, J. W. (British Empire Cancer Campaign Res. Lab., U. Nottingham, England). *Europ J Clin Biol Res* 5(6):593-598, 1970.

Chemically-induced tumors frequently possess new antigens, which have been described as tumor-specific transplantation antigens because of their capacity to elicit rejection responses against transplanted tumor cells in syngeneic hosts. Tumor-specific antigens with identical specificities have been demonstrated in some cases by *in vitro* interaction of tumor cells with humoral antibody or sensitized lymphoid cells. These antigenic specificities differ from those of antigens on virus-induced tumors where cross-reactivity is a common feature. It is now evident, however, that virus-induced tumors may also have tumor antigens with individual specificities. Tumor-specific antigens in chemically-induced tumors can be considered as expressions of new genetic specificities induced by the carcinogen. Definition of their frequency of expression in tumors may, therefore, indicate the number of cellular receptors modified during chemical carcinogenesis. Although there is no evidence that these antigens play any direct role in neoplastic transformation, other than their influence in displacing the array of normal cell surface antigens, they undoubtedly affect tumor growth potential. (67 references)

0362 RECENT ADVANCES IN IMMUNOLOGIC DIAGNOSIS OF DIGESTIVE CANCER. (E.) Zamcheck, N. (Boston City Hosp., Mass.) and A. Stillman. *Amer J Dig Dis* 15(11):1003-1018, 1970.

Immunologic methods have been developed which can detect minute amounts of antigens which are specific for several cancers of the digestive system; these antigens include α -fetoglobulin, carcinoembryonic antigen, gastric juice sulfoglycoproteins, and "tumor glycolipids." α -Fetoglobulin has been detected in the serum of 68% of patients with hepatomas in 1 study; only 3.1% of patients without hepatoma who had other neoplasms were α -fetoglobulin-positive. It is common, however, for patients with hepatomas not to exhibit α -fetoglobulin. The frequency of α -fetoglobulin associated with hepatoma may be related to the agent inducing the tumor. Fewer Caucasian patients with hepatoma produce α -fetoglobulin than non-Caucasian patients; and newborn animals synthesize α -fetoglobulin only in negligible amounts. Carcinoembryonic antigen was found associated with tumors originating in the endodermally derived epithelium of the digestive system; cancers of the colon and rectum were most frequently involved, but duodenal tumors, stomach tumors, and tumors of the esophagus also showed concentrations of carcinoembryonic antigen. Studies have shown carcinoembryonic antigen in 97% of patients with colonic or rectal carcinomas. Gastric sulfoglycoproteins have been detected in 96% of patients with gastric cancer in 1 study; however, gastric sulfoglycoproteins are also found in patients with benign peptic ulcers, a finding which

limits the clinical usefulness of the antigen for diagnostic purposes. "Tumor glycolipids", specifically cytolipin G, have been found in tissues and tumors of the gastrointestinal tract. (112 references)

0363 DERMATOGLYPHICS IN LEUKEMIA. (E.) Rosner, F. (Maimonides Med. Ctr., Brooklyn, N.Y.). *Lancet* 2(7678):882-883, 1970.

Of 9 recent studies of the correlation of dermatoglyphic features and leukemia, 5 have reported that leukemic patients show significantly different dermatoglyphic characteristics than normal subjects; the differences usually involved increased radial loops and/or whorls on the fingers of leukemic patients and increased simian or Sydney lines on their hands. Two studies, however, reported that there was no difference between dermatoglyphic patterns in leukemia patients and in normal subjects and that data on specific dermatoglyphic parameters in leukemic patients and normal subjects are contradictory. It seems premature to conclude, on the basis of dermatoglyphic peculiarities, that there is evidence for a genetic or teratogenic factor controlling both leukemia and dermatoglyphic patterns. (14 references)

0364 LEUKEMIA IN TWINS: WORLD-WIDE REVIEW OF CLINICAL CASES. (E.) Keith, L. (Chicago Med. Sch., Ill.) and E. Brown. *Acta Genet Med Gemellol* 19(1-2):66-68, 1970.

From an extensive review of world-wide clinical reports of leukemia in twins, 62 cases were compiled and examined. Leukemia occurred in the Perinatal-Congenital period (birth to 1 yr) in 15 cases, in the Early Childhood period (2-7 yr) in 26 cases, in the Late Childhood period (7-12 yr) in 9 cases, and in the Adult period (remaining years) in 12 cases. Leukemia occurred in monozygous (MZ) twins in 39 cases (21 cases of concordance and 18 of discordance), in dizygous twins (DZ) in 13 cases (4 cases of concordance and 9 of discordance), and in the remaining 10 cases the zygosity was doubtful. Discordance became more prevalent in the later periods with the concordance-discordance ratio decreasing in MZ sets (10:1, 6:6, 1:5, and 4:6) and in DZ sets (1:1, 3:5, 0:1, and 0:2) for the Perinatal-Congenital, Early Childhood, Late Childhood and Adulthood periods, resp. (5 references)

0365 CANCER IN TWINS: CONCORDANCE OR DISCORDANCE? (E.) Keith, L. (Chicago Med. Sch., Ill.) and E. Brown. *Acta Genet Med Gemellol* 19(1-2):61-64, 1970.

Published reports (1940-1964) of cancer in twins were reviewed to point out the obvious limitations to concordance studies. Conclusions within publications from the same institution changed according to the period of observation. Materials and methods for determining zygosity were sometimes questionable, and the possibility that not all cases of

cancer in twins were reported must be considered. Small numbers of cases with categorized sites and types of tumors were used to produce general support for the theory that genetic factors operate either in the concordance of cancer on in the site of the specific tumors. Type, site, and age at onset of tumors apparently affected monozygous twins more frequently than both members of a dizygous pair. The exact genetic influence on concordance or even in the development of malignant growths is doubtful. (15 references)

- 0366 DIAGNOSIS AND THERAPY OF THOROTRAST-INDUCED TUMORS. (Ger.) Beckenbach, H. (German Cancer Res. Ctr., Heidelberg), G. Van Kaick and W. Wenz. *Z Krebsforsch* 74(4):318-328, 1970.

The late effects of thorotrast administration are reviewed through the available literature and the author's clinical experience (300 patients). Among the factors contributing to its effects are its long half-life (1.39×10^{10} yr), its radioactive emission products (90% α -, 9% β - and 1% γ -radiations), the accumulation of 15 μ -sized thorium dioxide particles and its failure to be excreted from liver, spleen, bone marrow and lymph nodes. Late effects included fibroses at the injection site after defective paravascular administration, diseases of the hematopoietic system (leukocytoses), and the occurrence of tumors 10-20 yr after thorotrast administration. The liver is considered to be the most susceptible organ to thorotrast carcinogenesis, accumulating approximately 50% of the intravascularly administered substance. Accumulation occurred mainly extracellularly in the area of Glisson's sheath, and led to liver cell carcinoma and bile duct carcinoma. (18 references)

- 0367 CANCER HAZARDS IN THE LABORATORY. (E.) Anonymous. *Brit Med J* 3(5718):298-299, 1970.

Hazardous carcinogenic compounds encountered by laboratory workers in the course of their duties include α - and β -naphthylamine, benzidine, 4-aminodiphenyl, orthodiansidine, 4-nitrodiphenyl, orthotolidine and salts of these compounds. High incidences of bladder cancer among laboratory workers who handle these chemicals on a large scale are suggested by an increasing number of individual case reports, and occupational exposure to carcinogenic compounds is implicated. A study of 3,367 death certificates of chemists showed that among male chemists from 20-64 yr-of-age, there were 444 deaths from cancer compared to 354 expected cancer deaths; 41 of the excess deaths were attributed to malignant lymphoma or to cancer of the pancreas. However, the above study did not find a significant excess of deaths from cancer of the urinary bladder, but the number of cases expected and found were small. (8 references)

- 0368 CANCER IN GYNECOLOGY AND OBSTETRICS. (Fr.) Simard, R. (Hosp. Notre Dame, Montreal, Quebec, Canada). *Un Med Canada* 99(11):2047-2050, 1970.

Epidemiological features of cervical cancer such as its higher incidence among the economically less privileged and among women of minority races, its association with sexual activity, vaginal infection and early marriage, its high frequency among prostitutes and its absence in the virgin female are reviewed. The incidence of this malignancy in Canada is highest in the Province of Quebec (according to 1967 data), where it approaches the incidence of cardiovascular diseases. The importance of detection of this disease in the preclinical stage is emphasized. (22 references)

- 0369 THE PROBLEM OF CARCINOMA OF BILHARZIAL BLADDER IN IRAQ: CRITICAL REVIEW. (E.) Talib, H. (Baghdad U., Iraq). *Brit J Urol* 42(5):571-579, 1970.

The incidence, clinical features, and treatment of carcinoma of the bladder and the correlation with bilharziasis among the inhabitants of Iraq is reviewed. Of 78 patients with carcinoma of the bladder evaluated during the past 3 years, 39 were squamous cell carcinoma (10 with bilharziasis), 2 were transitional cell carcinoma (2 with bilharziasis), and 9 were undetermined. The predominance of a bilharzial history with squamous cell tumor and the occurrence of only transitional cell tumor in patients from northern regions where bilharziasis is rare suggest the chronicity of a process which ultimately gives rise to metaplastic changes in bladder epithelium. The primary symptom was hematuria, but dysuria, increased urinary frequency, and renal colic were also observed. Treatment was based on several factors (the patient's condition and renal function, the stage of the illness, and coincidence of other diseases) and included surgery, transurethral resection, interstitial radiation, ray therapy, and chemotherapy. (13 references)

- 0370 CONSIDERATIONS CONCERNING RADIATION RISKS. (Ger.) Wachsmann, F. (Soc. Radiation R., Munich, Germany) *Radiologe* 10(9):345-353, 1970.

Difficulties in determining the optimal dosage of radiation in medical practice are discussed. Of particular concern are radiation-induced malignant tumors, such as thyroid gland and skeletal tumors, leukemias, genetic damage, injury to the embryo and other harmful consequences of radiation. The linear relationship of dose effect to damage is established, although the frequency of damage induced by radiation increases with the dose. A problem which has not been entirely solved is the question of the cumulative effects of radiation. It is recommended that the effects of accumulated doses should be taken into account in treatment. The risk of leukemia is particularly prominent in radiologists, and also in patients whose treatment necessitated radiation. On the other hand, it is of interest to note the low frequency of leukemia in children whose mothers were exposed to radiation during their pregnancies. The atomic bomb explosion in Japan precipitated many malignant tumors in older people, far outnumbering those found in the young. Other effects of exposure to whole body radiation are discussed. (35 references)

0371 RIOPELLE'S TUMOR: II. HISTOGENESIS AND CONCLUSIONS. (Fr.) Roujeau, J. (Hosp. Pariboisiere, Paris, France) and A. Galian. *Ann Anatol* 4(3):149-157, 1970.

The theories on the histogenesis of Riopelle's tumor are reviewed and illustrated by morphological data obtained from dimethylnitrosamine-induced kidney tumors in rats and by an analysis of kidney embryology. The classical theories attributing an embryonic origin to these tumors due to their morphological resemblance to embryonic renal tissue are being challenged by more recent views attributing a neural origin to these tumors. This latter view is supported by the frequent occurrence of primary nerve tumors in the kidney. It is concluded, however, from the morphological data, that Riopelle's tumor constitutes an adult equivalent to Wilms' tumor, possibly originating from a single cell strain endowed with a double epithelial and connective tissue potentiality. (49 references)

0372 HORMONE PROFILES AND DISCRIMINANT FUNCTIONS IN CANCER. (E.) Anonymous. *Lancet* 2(7682):1070-1071, 1970.

Various studies have attempted to determine hormonal factors which constitute "discriminant functions" in a compiled statistical data on the clinical pictures presented by cancer patients. A particular variable analyzed is said to be a discriminant function if it effectively picks out cancer patients from controls and accentuates the differences between them. It has been shown that high etiocholanolone relative to 17-hydroxycorticosteroids is a discriminant function for patients with advanced breast cancer; in a related study, corticotrophin-stimulated levels of urinary 17-oxosteroids and 17-hydroxycorticosteroids successfully separated cancer patients responsive and unresponsive to adrenalectomy. In patients with breast, prostate and lung cancer effective discriminants have been based on gonadotrophin, estriol and androsterone values. Abnormal urinary excretion of such hormones as androsterone, etiocholanolone, and pregnanediol discriminate lung cancer patients from well and emphysematous controls. The findings of hormonal abnormalities associated with cancer suggests that the following factors contribute to the overall hormonal profile of patients: underlying endocrine abnormalities which arise independently of the onset of cancer; effects of illness as the disease progresses; and tumor metabolism. (18 references.)

0373 NASAL PAPILLOMATOSIS. (E.) Kusiak, R. J. (Durham, N. C.) and W. R. Hudson. *Southern Med J* 63(11):1277-1280, 1970.

The histology and pathogenesis of nasal papillomas were investigated in a review of the literature of this condition and in a survey of hospital cases. Nasal papillomatosis comprises 5 conditions, including common polyp (or soft papilloma), papillary squamous cell carcinoma, hyperkeratotic papillary growths, septal papillomas and inverted papillomas.

Hyperkeratotic tumors arose only from the stratified squamous epithelium of the nasal vestibule, while the other lesions were derived from the pseudostratified columnar epithelium lining the nasal cavity. Both septal and inverted papillomas were covered by epithelium ranging in type from columnar to squamous; hyperplastic epithelium in inverted papilloma tended to grow inward simulating stromal invasion. In more malignant papillomas, the underlying soft tissue or the bone was invaded. Nasal papillomatosis is a rare condition which usually arises in men during their fifth or sixth decade. The etiology of nasal papillomas is unclear, but there is evidence for a viral agent. (19 references)

0374 MIXED CALCIFIED ODONTOGENIC TUMORS. (E.) Stasinopoulos, M. (Athens, Greece). *Brit J Oral Surg* 8(1):93-100, 1970.

The classification and development of mixed calcified odontogenic tumors were examined on the basis of a study of 201 cases and a review of the relevant literature. The thesis that these tumors result from trauma was rejected, as only 4 of the 201 cases studied had any relation to trauma. Mixed calcified odontogenic tumors develop during the period of odontogenesis only; no case was found where tumors developed after this period. Of 190 cases, 103 were males and 87 females. Tumors classified as complex composite odontoma showed a predilection for the area of the lower molar teeth (35 cases), while compound composite odontoma were most common in the region of the upper anterior teeth (55 cases). On gross examination odontoma showed atypical calcified masses or clusters of denticles, while microscopically, tumors were composed of enamel and 1 or more of the other dental tissues. Tumors rarely affected the first or deciduous teeth (4 of 201 cases), and often showed a prolonged latent period intervening between development and onset of presenting symptoms, which included pain and swelling. (34 references)

0375 PUBERTY AND CANCER. (E.) Anonymous. *Brit Med J* 3(5725):722-723, 1970.

The peak in the death rate for acute myeloid leukemia at age 17 in males and somewhat earlier in females may be attributed to the accelerated bone growth in adolescence. However, it may be that the peaks in myeloid leukemia deaths during adolescence represent an acceleration of a carcinogenic process which, without increased bone growth in adolescence, would have proceeded at a more leisurely pace and manifested itself later in life. It is not clear whether reports of peaks in death rates from neuroblastomas, Wilm's tumor, and lymphatic leukemias in children and mothers exposed to x-rays during pregnancy correspond to periods of maximal bone growth. The observed peaks in death rates following puberty may result from temporary alterations in the body's defenses against carcinogens to which it had been exposed caused by rapid growth at puberty. (4 references)

- 0376 CAMPAIGN AGAINST CANCER. (E.) Anonymous.
Brit Med J 3(5715):118-119, 1970.

A brief digest of the contents of the 47th Annual Report of the British Empire Cancer Campaign surveys carcinogenesis research presently going forward under the auspices of the Campaign. It has been demonstrated that some carcinogens, administered during pregnancy, are teratogenic; however, a close association between carcinogenesis and teratogenicity is not apparent. An examination of children with solid tumors in one London hospital has shown that, apart from an increase in malformations of the lower gastrointestinal and urinary tracts in patients with sacrococcygeal teratoma, none of the groups of neoplasms was associated with a conspicuous increase in congenital abnormality. Another study has demonstrated that infection with a mycoplasma renders rats susceptible to the stimulation of cell proliferation in the tracheobronchial epithelium by tobacco smoke. The antitumor activity of 5-aziridino-2,4-dinitrobenzamide against certain transplantable tumors may or may not be of clinical significance. The enzyme L-asparaginase derived from *E. coli* has been shown to be effective in lowering the blast cell count in patients with acute myeloid or acute lymphoblastic leukemia. Males with Klinefelter's syndrome may have a 20-fold increase in incidence of breast cancer compared to the normal population, a conclusion based on a study of 68 cases of Klinefelter's syndrome. Detritus from 2 vitallium articulatory surfaces rubbed together mechanically in Ringer's solution gave rise to a rhabdomyosarcoma after intramuscular injection in rats. Eighty percent of biopsy specimens taken some distance from transitional-cell carcinomas of the bladder showed changes which were interpreted as precancerous. (3 references)

- 0377 INTERNATIONAL RESEARCH: ITS ROLE IN ENVIRONMENTAL BIOLOGY. (E.) Higginson, J.
(Inst. Agency Res. Cancer, Lyon, France). *Science* 170(3961):935-939, 1970. (11 references)

- 0378 CONSIDERATIONS ON THE CARCINOGENIC ACTIVITY OF CYCLAMATES. (Fr.) Rudali, M. G. (Curie Found., Paris, France), E. Coezy and M. I. Muranyi-Kovacs. *Lutte Contre Cancer* 47(180):16-19, 1970.

- 0379 THE CYTOLOGICAL FEATURES OF MALIGNANCY. (Ger.) Petrow, Z. D. (1st Med. Clin., Humboldt U., Berlin, Germany) and H. Stobbe. *Z Aertzl Fortbild* 64(18):931-939, 1970. (5 references)

- 0380 CANCER OF THE URINARY TRACT. (E.)
Clayson, D. B. (Sch. Med. Leeds, England) and E. H. Cooper. *Advances Cancer Res* 13:271-381, 1970. (399 references)

- 0381 VIRUS AND CANCER. (Sp.) Vicente, J.
(Jimenez Diaz Found., Madrid, Spain). *Rev Clin Espagn* 118(5):395-408, 1970. (150 references)

- 0382 THE RADIOACTIVE FACTOR OF TOBACCO SMOKE. (Rus.) Nikolova, M. E. (Bulgaria) *Gig Sanit* 35(8):89-93, 1970. (42 references)

- 0383 LUNG CANCER AND AIR POLLUTION DUE TO INDUSTRIALIZATION. (It.) Vagnoni, G.
(Inst. Chir., U. Catania, Italy). *Gazz Int Med Chir* 75(15):1160-1172, 1970. (28 references)

- 0384 THE ACTIVITIES OF THE LYON INTERNATIONAL AGENCY IN THE INVESTIGATION OF ECOLOGICAL CARCINOGENIC FACTORS. (Rus.) Bogovsky, P. A. (n affil). *Vop Onkol* 16(8):91-96, 1970. (6 references)

- 0385 THE ROLE OF HORMONAL DISORDERS IN THE ETIOLOGY OF TUMORS. (Rus.) Lipschutz, (Inst. Exper. Med. Minist. Publ. Hlth., Santiago Chile). *Vop Onkol* 16(6):94-104, 1970. (44 references)

- 0386 COMPOSITION AND USE OF PEANUTS IN THE DIET. (E.) Woodroof, J. G. (U. Georgia Coll. Agric. Exp., Georgia, Ga.). *World Rev Nutr Diet* 11:142-169, 1970. (29 references)

- 0387 OILSEED PROTEIN: PRESENT AND FUTURE. Woodham, A. A. (Rowett Res. Inst., Aberdeen, Scotland). *World Rev Nutr Dietetics* 11:44-76, 1969. (41 references)

- 0388 FUNGAL TOXINS. (E.) Lillehoj, E. B. (n affil), A. Ciegler and R. W. Detroy. *Essay Toxicol* 2:1-136, 1970. (640 references)

- 0389 EVIDENCE FOR THE VIRAL ETIOLOGY OF LEUKEMIA IN THE DOMESTIC MAMMALS. (E.) Jarrett, O. (U. Glasgow, Anim. Leukemia Res. Unit Scotland). *Advances Cancer Res* 13:39-62, 1970. (96 references)

0390 THE CHARACTERISTICS OF ANIMAL CELLS TRANS-
FORMED *IN VITRO*. (E.) MacPherson, I.
(Imperial Cancer Res. Fund Lab., London, England).
Advances Cancer Res 13:169-213, 1970. (233 refer-
ences)

0391 LYMPHOCYTE PROLIFERATION AND LYMPHO-
PROLIFERATIVE DISORDERS. (E.) Rubin, A.
D. (Mount Sinai Sch. Med., New York, N.Y.), L. I.
Johnson and S. M. Brown. *Progr Exp Tumor Res* 13:
135-180, 1970. (201 references)

0392 EPIGENETIC PROCESSES AND THEIR RELEVANCE
TO THE STUDY OF NEOPLASIA. (E.) Sherbet,
G. V. (Roy. Cancer Hosp., London, England). *Advan-
ces Cancer Res* 13:97-167, 1970. (245 references)

0393 IMMUNOPATHOLOGY AND NEOPLASMS IN NEW
ZEALAND BLACK (NZB) AND SJL/J MICE. (E.)
East, J. (Imp. Cancer Res. Fund., London, England).
Progr Exp Tumor Res 13:84-134, 1970. (120 refer-
ences)

- 0394 IMMUNOGLOBULIN CHANGES IN MICE WITH EXPERIMENTAL PLASMACYTOMA. (E.) Hashimoto, N. (Jikei U. Sch. Med., Tokyo, Japan). *Acta Haem Jap* 33(1):16-27, 1970.

The changes in immunoglobulin in mice with experimentally induced plasmacytoma (Freund's adjuvant, i.p.) were followed by immunoelectrophoresis. Sixteen wk after the first injection of adjuvant, the immunoglobulins in the sera showed bifurcation of the γ -precipitin line in the β -region, extending anodally (mid- γ bifurcation) in only 9 out of 20 animals; after 20 wk, 18 out of 19 animals showed this mid- γ bifurcation with 1 animal evidencing abnormal precipitin lines. At this stage (20 wk) plasma cells were inflammatory and reactive. After 42 wk, 3 mice showed the monoclonal pattern identified as M-component and excreted Bence Jones protein in the urine, and the plasma cells were atypical. Blood taken periodically (retro-orbital puncture of the ophthalmic venous plexus) from mice indicated that at 36 wk the bifurcation of 7S γG_1 and 7S γG_2 precipitin lines was evident, and at 42 wk the 7S γG_1 precipitin line increased while the 7S γG_2 became dimmer; at 44 wk the M-component seemed to be formed.

- 0395 DEVELOPMENT OF PLASMA CELL TUMOR IN BALB/c MICE: FROM CYTOHISTOLOGICAL ASPECTS. (E.) Okazaki, E. (Niigata U. Sch. Med., Japan). *Acta Haem Jap* 33(1):28-36, 1970.

The cytohistological development of plasma cell tumors (induced by Freund's complete adjuvant mixed with bacterial α -amylase or Taka-amylase, i.p.) was observed in 20 BALB/c mice. The predominant tumor cells fell into 3 distinct classes (mature plasma cells, anaplastic plasma cells, and reticulum cells), and no definite correlations between the monoclonal immunoglobulins synthesized and the class of cells could be made. Three of the animals exhibited plasma-cellular lesions in the early stages of development. The neoplastic cells were polygonal in shape with round or ovoid nuclei centrally located and were surrounded by delicate reticulin fibers. Chronological observations at 1 wk intervals after injection with the antigen-adjuvant mixture disclosed scattered opaque spots on the peritoneal surfaces after 1 wk and small granulomatous lesions over the peritoneal and mesenchymal surfaces after 2 wk. After 5 wk mesenchymal cells (possibly histiocytic in origin) were found in clusters among the fatty droplets in the oil granulomas; after 8 wk round cells with large round nuclei and abundant pale blue cytoplasm, and round cells with eccentric chromophilic nuclei and dark blue cytoplasm were observed as well as leucocytic and lymphocytic cells.

- 0396 VIRUS-LIKE PARTICLES IN DEVELOPING PLASMA CELL TUMORS INDUCED IN BALB/c MICE. (E.) Scholle, R. H. (Walter G. Zoller Mem. Dent. Clin., U. Chicago, Ill.) and J. W. Foft. *Exp Molec Path* 13(2):147-158, 1970.

Virus-like particles were detected early in plasma cell tumors induced in BALB/c mice by mineral oil

injections. Mice were given 1 or 3 i.p. injections of 0.5 ml mineral oil at 1-4 months of age. Electron microscopic examination of an oil granuloma 1 animal revealed intracisternal A-type virus-like particles 12 days after 1 oil injection. Particles approximately 70 m μ in diameter with a doughnut shape with an electrolucent core were found in blast cells. In a second animal killed 12 wk after an injection of oil, particles were found in blast cells and in mature plasma cells. Neither the mice harboring virus-like particles had ascites and neither had definite plasmacytomas. In both cases, particles were seen budding from the endoplasmic reticulum of cells. The induced granulomatous tissue in which particles were found may provide a favorable environment for the morphological expression of an incomplete viral genome which be present in all mice of the strain tested. An etiologic role for viruses is suggested by the association of these particles with neoplastic plasma cells.

- 0397 INVESTIGATION OF BIOSYNTHETIC FORMATION OF POLYCYCLIC HYDROCARBONS IN HIGHER PLANTS. VIII. CARCINOGENIC HYDROCARBONS IN THE MAN-MADE ENVIRONMENT. (Ger.) Grimmer, G. (U. Hamburg, Germany) and D. Düvel. *Z Naturforsch* 25(10):1171-1175, 1970.

In order to study the environmental contribution to the carcinogenic chemical contents in plants, the polycyclic hydrocarbon levels in lettuce, rye, bean and tobacco plants grown outdoors, in a no greenhouse, and in a controlled climate chamber (fine dust and gas filtered air) were compared. The results demonstrated that none of the 7 polycyclic hydrocarbons (benzo(e)pyrene, benzo(a)pyrene, perylene, anthracene, benzo(ghi)perylene, dibenz(a,h)anthracene and coronene) tested for appearance in the plants grown in the controlled climate chamber. The plants grown both outdoors and in greenhouse from the same seeds showed considerable quantities of these carcinogens, although the controlled climate chamber was situated within a distance of 100 m from the other two test areas. Lettuce and soybeans had approximately 4 μ g/kg benzo(a)pyrene and similar levels of benzo(a)pyrene; rye had 3.4 μ g/kg benzo(e)pyrene and 1.6 μ g/kg benzo(a)pyrene; and tobacco plants had 2.5 μ g/kg benzo(a)pyrene and 1.8 μ g/kg benzo(a)pyrene.

- 0398 LOCAL VASCULAR CHANGES INDUCED BY THE CARCINOGEN, PHORBOL MYRISTATE ACETATE. Janoff, A. (New York U. Sch. Med., New York), A. Klassen and W. Troll. *Cancer Res* 30(10):2568-2571, 1970.

Vascular reactions in the ear skin of mice produced by phorbol myristate acetate, a cocarcinogen, were studied. Mice were given i.v. injections of 1 μ g of labeled bovine serum albumin, and i.v. injections of carbon suspension. One μ g of phorbol myristate acetate, produced a severe, local vascular reaction consisting of hyperemia and edema formation within

was quantitatively monitored by measuring uptake of circulating ^{125}I -labeled serum albumin. Microscopic detection of sites of endothelial injury in mice receiving i.v. carbon suspension showed the reaction to be primarily limited to venules. These microvascular changes were accompanied by mast cell degranulation in the affected tissues. Reactions developed about 1 hr after phorbol ester application, persisted through 6-8 hr, and appeared to be lessening in intensity by 24 hr. High doses (50 μg) of 7,12-dimethylbenz(a)anthracene induced similar vascular changes, although of much lower intensity and after a longer delay interval. Antagonists of histamine, serotonin, and kinins produced mild, transient suppression of the local vascular response to the phorbol ester. Hydrocortisone and salicylate were without effect on this component of the tissue reaction. A more sustained protection against the inflammation by phorbol ester was provided by local application of tosyl phenylalanine chloromethyl ketone, a protease inhibitor previously shown to suppress tumor promotion.

0399 PRODUCTION OF HEPATOMAS IN SUCKLING MICE AFTER SINGLE APPLICATION OF β -PROPIOLACTONE. (E.) Chernozemski, I. N. (Oncol. Res. Inst., Sofia, Bulgaria) and G. P. Warwick. *J Natl Cancer Inst* 45(4):709-717, 1970.

Male and female mice of various ages were given i.p. injections of 0.1 mg/g body wt β -propiolactone; suckling mice received topical applications of 0.6 mg/g body wt of the same compound. Mice receiving β -propiolactone injections on the 8th-10th day after birth developed an average of 2 hepatomas per animal in 65% of the males 16 months after treatment. In adult mice, olive oil-treated and untreated controls, the incidence of hepatomas was 9%, 4% and 6.7%, resp. Of the suckling mice which were treated with topical applications, 19.4% of the animals developed hepatomas. Treated females developed few hepatomas, though 16-20% bore malignant lymphomas (5.5% in controls). The hepatomas were trabecular or solid, and showed no metastasis to sites other than the liver, although hematopoietic embryonal cells and tumor cell embolism were observed.

0400 DETERMINATION OF THE MUTAGENIC ACTIVITY TO BACTERIOPHAGE T4 OF CARCINOGENIC AND NON-CARCINOGENIC COMPOUNDS. (E.) Corbett, T. H. (Oak Ridge Natl. Lab., Tenn.), C. Heidelberger and W. F. Dove. *Molec Pharmacol* 6(6):667-679, 1970.

The mutagenic activity of 41 carcinogens (assumed to be in the active forms) and 4 non-carcinogens and the types of mutational events produced by the active compounds were studied in bacteriophage T4. No toxicity to *Escherichia coli* BB was observed in a bacterial assay at maximal concentrations for 25 of the carcinogens so that they were presumed to be non-mutagenic. Four inorganic salts (nickel sulfate, cobalt nitrate, calcium chromate, and lead acetate) and 5 chemical carcinogens (N-hydroxy-1-naphthylamine, N-hydroxy-2-naphthylamine, N-hydroxy-2-aminofluorene, 10-formyl-1,2-benzanthracene, and DL-ethionine) were toxic but not mutagenic to intra-

cellular T4 phage. Six reactive carcinogens were mutagenic to T4 phage: β -propiolactone (producing frameshift, GC to AT, AT to GC, and the nonsense mutations amber, ochre, and UGA as well as large deletions), propane sultone (producing all except the ochre nonsense mutation), N-acetoxy-2-acetylaminofluorene and 7-fluoro-N-acetoxy-2-acetylaminofluorene (producing frameshift, AT to GC, UGA, and amber mutations as well as large deletions), glyceraldehyde (producing frameshift, AT to GC, GC to AT, and UGA mutations as well as large deletions), and nitrogen mustard (producing frameshift, GC to AT, and UGA mutations as well as large deletions).

0401 CARCINOGENICITY OF TWO N-DIAZOACETYL-DERIVATIVES OF GLYCINE IN THE NEWBORN SWISS MOUSE. (It.) Brambilla, G. (Inst. Pharmacol., U. Genoa, Italy), M. Cavanna, S. Parodi and C. E. Caraceni. *Boll Soc Ital Biol Sper* 46(5):227-230, 1970.

The incidence of lung adenomas and leukemias induced by N-diazoacetylglutylglycinamide (DGA) and N-diazoacetylglutylglycine hydrazide (DGH) was studied in newborn randombred albino Swiss mice. Both DGA and DGH were administered i.p. in doses of 180, 300 and 500 mg/kg daily for 4 consecutive days to 48-72 hr-old baby mice. The animals were weaned and sex-segregated at 30 days-of-age. The mortality within this period for the experimental animals was 15 and 8 (180 mg/kg), 15 and 9 (300 mg/kg) and 66 and 50% (500 mg/kg) for DGA and DGH, resp., and 6% for the control group. The surviving animals were sacrificed at 180-200 days-of-age. The incidence of lung adenoma was 100% in all treated groups with increasing average numbers of neoplastic nodules per lung with the increasing treatment doses; no differences between the effects of the 2 compounds were noticed. The incidence of lung tumors in the control group was 4% at 6 months-of-age. Development of leukemia was dose-dependent for both compounds: DGA seemed to be more active, producing leukemia in 10%, 43% and 71% of the animals treated with 180, 300 and 500 mg/kg, resp., than DGH which produced leukemia in 5%, 16% and 71% of the animals at the above doses, resp. A marked enlargement of the thymus, spleen and lymph nodes and leukemic infiltrations of the liver and kidney were noticed in most of the leukemic animals. No sex differences were observed in the susceptibility towards the 2 compounds. The mechanism of carcinogenesis was attributed to the alkylating action of these compounds, possibly associated with their known immunosuppressive effects, particularly in the case of N-diazoacetylglutylglycinamide.

0402 CARCINOGENICITY OF STERIGMATOCYSTIN. (E.) Purchase, I. F. H. (South African Med. Res. Council, Pretoria) and J. J. Van Der Watt. *Food Cosmet Toxic* 8(3):289-295, 1970.

Weanling rats of both sexes were fed (via gavage) or in the diet the mycotoxin sterigmatocystin in doses of 0.15-2.25 mg/day for 1 yr in order to investigate the carcinogenic properties of this

agent. Eight rats which received a high dose (1.5-2.25 mg/day) of sterigmatocystin died between wk 5 and 18, while 39 out of the 50 treated rats surviving to wk 42 eventually developed hepatic carcinoma. Of these, 31 had varying degrees of fibrosis. Eight tumours of other types were seen in the liver, uterus, ovary, spleen or omentum, and acanthotic changes occurred in the stomachs of 85% of the treated rats. The lesions produced in the livers of rats exposed to sterigmatocystin are similar to those found in Bantu hepatoma and 'toxic' hepatitis. Dietary mycotoxin may be related to the high rate of liver cancer in Africa.

0403 NEOPLASTIC SEQUELAE FOLLOWING SUBCUTANEOUS IMPLANTATION OF MICE WITH RARE EARTH METALS.

(E.) Ball, R. A. (Vetr. Med. Inst., Iowa St. U., Ames), G. Van Gelder, J. W. Green, Jr. and W. O. Reece. *Proc Soc Exp Biol Med* 135(2):426-430, 1970.

Weanling mice were implanted s.c. with 200 mg pellets of gadolinium or ytterbium, and the development of tumors in these animals and in sham-operated controls was observed. Three of 60 mice treated with gadolinium and 9 of 58 mice treated with ytterbium developed sarcomas at the implantation sites. Pulmonary metastases occurred in 4 of the ytterbium-induced sarcomas. In addition, approximately 40% of the earth-metal treated animals and 50% of the control animals developed spontaneous neoplasms, most of which were bronchial adenomas. Possibly the heavy metals promote sarcomas by uncovering latent oncogenic factors; however, the mechanism associating heavy metal implantation and carcinogenesis in these experiments remains speculative.

0404 LYSOPINE AND OCTOPINE PROMOTE CROWN-GALL TUMOR GROWTH *IN VIVO*. (E.) Lippincott, J. A. (Dept. Biol. Sci., Northwestern U., Evanston, Ill.) and B. B. Lippincott. *Science* 170(3954):176-177, 1970.

Primary leaves of bean plants were inoculated with cells of a strain of the tumorigenic *Agrobacterium tumefaciens* and subsequently treated with varying (1-20 µg/leaf) amounts of lysopine (N-α-(1-carboxy-ethyl)-L-lysine) or octopine (N-α-(1-carboxy-ethyl)-L-arginine) to investigate the ability of these compounds to promote the growth of crown-gall tumors. A detectable response was observed when 1 µg/leaf of these compounds was added, and the mean volume of the tumors was increased 2-3-fold when greater amounts were applied. The specificity of the response and the unique association of these compounds with the tumors suggest that endogenous lysopine and octopine contribute to the growth characteristics of these tumors. However, lysopine and octopine are not tumorigenic *per se*, and the identity of the substances which initiate crown-gall tumors is unknown.

0405 CHANGES IN THE NUMBER OF BONE MARROW CELLS AFTER A SINGLE INJECTION OF METHIONINE SULFOXIMINE AS COMPARED WITH THE EFFECT OF WHOLE BODY IRRADIATION WITH X-RAYS IN MICE. (E.) Zak, (Med. Fac. Charles U., Prague, Czechoslovakia) and J. Kolousek. *Neoplasma* 17(4):339-343, 1970.

Male rats were administered either 400 mg i.p. injections of DL-methionine sulfoximine or 600 of whole-body X-irradiation to test the effect of these treatments on the number of bone marrow cells in the femoral bones. Both methionine sulfoximine and X-irradiation produced a cyclical decrease in the number of bone marrow cells, with the former treatment producing a maximum decrease of 47% in bone marrow cells after 14 days as compared with controls, and the latter treatment producing a maximal decrease of 95% in bone marrow cells after 5 days. Partial regeneration by the 28th day after treatment increased the number of bone marrow cells to 70% and 50% of controls for methionine sulfoximine and X-irradiation, resp. The inhibition of bone marrow cell production by methionine sulfoximine may be due either to metabolic changes or to changes in the neurosecretory centers of the hypothalamus induced by this agent.

0406 BINDING OF RADIOACTIVE N-HYDROXY-ACETYLAMINOFLUORENE TO SYNTHETIC POLYRIBONUCLEOTIDES. (E.) Marroquin, F. (Mead Johnson Ctr., Evansville, Ind.) and N. Coyote. *Chem Bio Interact* 2(2):151-153, 1970.

The binding of 9-¹⁴C-N-hydroxyacetylaminofluorene to synthetic polyribonucleotides was studied. The labeled carcinogen was incubated with 25 mg of soluble rat liver fraction and copolymer of guanylylidylic acid (G:U). The *in vitro* system was able to bind the radioactive carcinogen to the copolymer and the binding reaction did not occur when the preparation was boiled. As the concentration of the carcinogen in the incubation mixture was increased, the binding to copolymer G:U increased. Binding rates measuring 555 and 1280 cpm/20 µm absorbance at 260 nm for carcinogen concentrations of 0.025 and 0.200 µmoles, resp. In a comparative study copolymer G:U was able to bind 42% more N-hydroxyacetylaminofluorene than copolymer G and 12-fold more than polymers of inosinic, adenylylidylic or uridylic acids.

0407 FURTHER EVIDENCE FOR TWO TYPES OF ADENYLIC ACID IN N-HYDROXY-2-FLUORENYLACETAMIDE WITH RAT-LIVER PROTEINS. (E.) Barry, E. J. (VA Hospital, Minneapolis, Minn.) and H. R. Gutmann. *Chem Bio Interact* 2(2):158-159, 1970.

The integrity of the amide linkage of protein products from the liver of rats given a single dose of N-hydroxy-2-fluorenylacetamide (N-OH-FAA, 1 mg, i.p.) throughout the isolation procedure was tested using N-OH-(1-¹⁴C)FAA. Half of the homogenized rat liver (taken 12 hr after injection) was immediately heated in boiling water for 15 min.

homogenate A) while the other half was maintained at 4°C for 4-5 hr (to simulate the isolation conditions) before boiling (homogenate B). The labeled acetic acid was recovered by the addition of sodium acetate (0.40 g) and monosodium phosphate monohydrate (1.4 g) to the homogenates, titration to pH 7.0, and steam distillation (control experiments indicated that hydrolysis of the N-acetyl group was very low under these conditions), and the titrable acidity of each distillate accounted for 24-28% of the carrier. The amount of radioactive acetic acid in homogenate A was 3.4% and in homogenate B was 6%, indicating that the amide linkage was stable during the isolation of the adducts and that the protein and nucleic acid adducts that did not retain the acetyl group observed after the administration of N-OH-FAA were not artifacts of the isolation procedure.

08 EFFECT OF ACETAMIDOFLUORENE AND ACTIVATED DERIVATIVES ON "MACROMOLECULAR SYNTHESIS" IN SINGLE CELL CULTURES. (E.) Süß, R. (German Cancer Res. Ctr., Heidelberg), V. Kinzel, M. Volm, K. Süß and J. Scribner. *Z Krebsforsch* 74(4):338-343, 1970.

Hamster embryo cells were incubated with acetoxy-, hydroxy-, or acetamidofluorene in final concentrations of 10^{-4} - 10^{-5} molar, and radioactive thymidine, uridine or leucine were added simultaneously to the cultures; the aim was to investigate effects of acetamidofluorene and its activated derivatives on macromolecular synthesis in the cell cultures as measured by the incorporation of the radioactive precursors. Precursor incorporation was reduced by 1-3 test compounds. Thymidine incorporation was reduced to 25, 25, and 5% of control values, respectively, for acetamidofluorene, N-hydroxyacetamidofluorene and acetoxyacetamidofluorene; leucine incorporation was reduced to 90, 85 and 5% of control values, respectively, by these compounds. Uridine incorporation was reduced to 80, 60, and 30% of control values, respectively. These findings correspond to the observed carcinogenic effects of the 3 compounds, of which acetoxyacetamidofluorene is the most active. As measured by precursor incorporation, DNA and RNA synthesis were more affected by the 3 test compounds than protein synthesis. Cells of the protozoan *Trichomonas pyriformis*, which were treated as were the hamster cells, showed the most significant RNA and DNA inhibition values for acetamidofluorene; in these cells, protein synthesis was virtually unaffected by any of the test compounds.

09 CHRONIC TOXICITY OF AZATHIOPRINE AND THE EFFECT OF THIS IMMUNOSUPPRESSANT ON LIVER TUMOR INDUCTION BY THE CARCINOGEN N-HYDROXY-N-2-FLUORENYLACETAMIDE. (E.) Frankel, H. H. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), S. Yamamoto, E. K. Weisburger and J. H. Weisburger. *Toxic Appl Pharmacol* 17(2):462-480, 1970.

The toxicity of chronic feeding of azathioprine and its effects on N-hydroxy-N-2-fluorenylacetamide (N-OH-FAA)-induced liver tumors were studied in male

and female Fischer F344 strain rats. Compared to control rats fed Wayne Laboratory Meal, the body weights dropped slightly for rats fed azathioprine (150 ppm), markedly for those fed N-OH-FAA (160 ppm), and were lowest for those fed a combination of both. In male rats azathioprine alone produced a normal hepatic structure with scattered enlarged parenchymal cells with watery cytoplasm; N-OH-FAA alone produced mildly nodulated liver surfaces and 9 out of 12 rats had well-differentiated hepatocellular carcinomas. The combination produced carcinomas which were difficult to differentiate in the multinodular livers (microscopically a marked increase of collagenous tissue was seen surrounding various types of parenchymal cell carcinomas). In female rats N-OH-FAA alone caused only minimal periportal fibrosis, but the combination produced a severe fibrotic reaction. The mixture of carcinogen and immunosuppressant appears to increase the toxic reaction to the liver but has no effect on the carcinogenic reaction.

0410 BINDING OF POLYCYCLIC AROMATIC HYDROCARBONS TO POLYADENYLIC ACID. (E.)

Craig, A. M. (Dept. Biochem, Biophys, Oregon St. U., Corvallis) and I. Isenberg. *Proc Nat Acad Sci* 67(3):1337-1344, 1970.

The hypothesis that some polycyclic hydrocarbons cannot bind to polyadenylic acid because their size prevents them from intercalating with the helical strands of the polyadenylic acid molecule was tested by model-building and actual binding experiments. Model building suggested that those hydrocarbons which do bind to the double-stranded, acid form of polyadenylic acid satisfy a size criterion allowing them to intercalate with the polyadenylic acid helix, thus being well protected from contact with the aqueous medium; hydrocarbons that are too large to be so protected were found not to bind. A size criterion for hydrocarbon binding to DNA was also tested. Binding experiments confirmed the size-criterion hypothesis; hydrocarbons which were predicted not to bind with polyadenylic acid, including 1,2,3,4-dibenzanthracene, pentacene, 9-phenylanthracene and 1,2,5,6-dibenzpyrene failed to bind. DNA binding hypotheses were also confirmed; 1,2,5,6-dibenzanthracene and tetracene failed to bind to DNA, and 1,2,3,4-dibenzanthracene did bind to DNA but not to polyadenylic acid. The findings appear to support the hypothesis that binding of polycyclic hydrocarbons to polyadenylic acid and to DNA is effected by intercalation, and that hydrophobic interactions are dominant in the binding process.

0411 TWO NEW TYPES OF SARCOMA INDUCING HETEROCYCLIC COMPOUNDS: BENZOCARBOLINES AND THIENOPYRIDOCARBAZOLES. (Fr.) Lacassagne, A. (Inst. Radium, Paris, France), N. P. Buu-Hoi, F. Zajdela, O. Perin-Roussel, P. Jacquignon, F. Perin and J. P. Hoeffinger. *C R Acad Sci* 271(16):1474-1479, 1970.

The oncogenicity of 15 newly synthesized heteropolycyclic compounds, 9 of which had only nitrogen

and 6 of which had both nitrogen and sulfur heteroatoms, was tested on C57BL mice. Each compound (0.6 mg) was injected s.c. 3 times at monthly intervals. Animals were sacrificed at the occurrence of the first tumor or day 553 of the experiment, and their principal organs including the tissue at the injection site were examined histologically. Two compounds which were oncogenic were 8,9-benzog-carboline, which induced sarcoma in 2 females after 301 and 346 days of latency), and 12H-pyrido[2,3-a]thieno[2,3-i]carbazole, which induced sarcomas in 3 out of 21 animals (14 males, 7 females) after 212 and 412 days of latency in the males and 276 days of latency in the female. No spontaneous tumor occurred in 4000 control animals over 500 days old. The first compound was structurally related to reserpine and constitutes the first alkaloid-like compound with oncogenic properties. The second compound was isosteric to 13H-benzo[*i*]pyrido[3,2-a]carbazole which is a strong carcinogen; apparently, substitution of benzene by a thiophene ring decreased considerably its oncogenic properties. The negative response to the other tested compounds seems to emphasize the importance of the position of the nitrogen within the pyridine ring in terms of carcinogenicity. Apparently, any increase in molecular weight of the heteropolycyclic skeleton (introduction of an additional benzene ring or methyl group or substitution of a benzene by a thiophene ring) leads to a decrease or removal of oncogenicity.

- 0412 THE GENETIC ACTION OF AROMATIC AMINES AND THEIR DERIVATIVES: INDUCTION OF MITOTIC CONVERSIONS IN THE YEAST *SACCHAROMYCES CEREVISIAE*. (Ger.) Marquardt, H. (Forest Botanical Inst. U. Freiburg, Germany), F. K. Zimmermann, H. Dannenberg, H. G. Neumann, A. Bodenberger and M. Metzler. *Z Krebsforsch* 74(4):412-433, 1970.

An investigation aimed at the characterization of the concept "genetic activity of a substance" was conducted to provide experimental data contributing to the disputed relationship between the action of a substance and its genetic activity. Derivatives of 2-aminofluorene, 4-amino-trans-stilbene and *p*-toluidine as well as 4-dimethylaminodibenzyl, *p*-nitroso- and *p*-nitrotoluene were tested for genetic activity (induction of mitotic gene conversion) in cells of yeast *Saccharomyces cerevisiae* (changes in single or a few nucleotide bases within one gene locus). N-Acetoxyacetylaminofluorene and N-acetoxyacetyl-amino-trans-stilbene were genetically strongly active as potentially ultimate carcinogens. With increasing sensitivity of the conversion system the proximal carcinogen N-hydroxyacetyl-amino-trans-stilbene still induced mitotic gene conversion, but the N-hydroxy-2-acetylaminofluorene was no longer active. The non-carcinogen and precarcinogen compounds were genetically inactive. The yeast cell was not able to N-hydroxylate the precarcinogens, acetylaminofluorene and acetyl-amino-trans-stilbene; among the toluidine derivatives only N-acetoxyacetyl-*p*-toluidide, acetyl-*p*-toluidine and its oxidation product *p*-nitrosotoluene were active. Besides the oxidation of the amino nitrogen the aromatic

nucleus also appears to be a controlling factor in genetic activity. Correlations between genetic activity and carcinogenicity were discussed in based on molecular mechanisms affecting base within gene loci.

- 0413 THE EFFECT OF CERTAIN MONO-FUNCTIONAL METHANESULPHONOXY-ALKANES ON HAEMOPOLYMER FORMING UNITS IN THE RAT. (E.) Dunn, R. (Roy. Cancer Hosp., London, England) and I. Elson. *Rev Europ Etud Clin Biol* 15(7):771-774, 1970.

The effects of methyl (MMS, 50 mg/kg, i.p.), ethyl (EMS, 175 mg/kg, i.p.), and isopropyl (IPMS, 500 mg/kg, i.p.) methanesulfonates on the number of hemopoietic colony forming units/femur (CFU/femur) and on peripheral blood neutrophil-lymphocyte ratio (N/L) were studied in female Wilkie hooded rats. The control value of CFU/femur (1400) was significantly increased by MMS (1750) and EMS (1600) and significantly decreased by IPMS (600) 48 hr after administration. When measured 24 hr after administration MMS significantly increased the CFU/femur (2050) from the control value (1400) but the increase was blocked by the simultaneous administration of (1 mg/kg, i.p.) of vinblastine sulfate (no significant effect when given alone). MMS, EMS, and IPMS depressed peripheral neutrophil-lymphocyte ratio (N/L of 10, 4.7, and 1.0, resp.).

- 0414 LUNG TUMORS INDUCED BY SMALL AMOUNTS OF HYDRAZINE SULFATE IN GONADECTOMIZED BALB/c/Se MICE. (It.) Biancifiori, C. (Dept. Cancer, U. Perugia, Italy). *Lavori Anat. Pat. Perugia* 30(2):113-119, 1970.

The effect of gonadectomy on hydrazine sulfate carcinogenesis was studied on BALB/c/Cb/Se mice grouped as follows: (A) control group of unoperated virgin animals (25 males and 25 females); (B) gonadectomized untreated animals (22 males and 22 females); (C) gonadectomized mice administered 0.56 mg of hydrazine sulfate daily or a total of 0.56 mg p.o. (24 males and 26 females); (D) gonadectomized mice treated with 0.56 mg of hydrazine sulfate (total of 84 mg), 0.28 mg (total of 42 mg) or 0.14 mg daily (total of 21 mg) consisting of 25 males and 24 females, 27 males and 21 females, and 28 males and 26 females, resp. Gonadectomy was performed at 6 wk of age and treatment started at 8 wk of age. Single spontaneous pulmonary tumors occurred in 24% of the male and 4% of the female of group A and in 9% of the male and 26% of the female mice from group B, resp. These animals died at 92-100 wk of age. Multiple (2-4) lung tumors occurred in 19 of 24 males (79%) and 19 of 24 females (79%) which died at 67-69 wk of age in group C. The incidence of lung tumors in group D was 75% after 74-76 wk, 63% and 81% after 77-79 wk and 54% and 57% after 76-80 wk, resp., in males and females according to the above described dosages.

- 15 LUNG AND LIVER TUMORS INDUCED BY SMALL AMOUNTS OF HYDRAZINE SULFATE IN BALB/c/Cb/ MICE. (It.) Biancifiiori, C. (Dept. Res. Cancer, Perugia, Italy). *Lav. Anat. Pat. Perugia*, 30(2): 99, 1970.

order to test the safety of the therapeutic use isoniazide in tuberculous patients, its chief metabolite, hydrazine sulfate, was administered to LB/C/Cb/Se mice, starting at age 8 wk. The incidence of spontaneous tumors (adenomas or/and carcinomas) in the nontreated group (25 males and 25 females) was 24 and 4%, resp. Multiple lung tumors (4/animal) developed in 90% of both males and females given 1.13 mg of hydrazine sulfate p.o. daily for a total of 170 mg each after a latency period of 59 and 64 wk, resp; no liver tumors occurred. In animals treated with 0.56, 0.28 and 0.14 mg daily (total dose-84, 42 and 21 mg, resp.), multiple tumors developed in 65% and 76%, 62% and 54%, and 54% and 32%, in males and females, resp. after a 72-78 wk latency period. Of animals subjected to short-term treatment (1.13 mg daily for 4 wk) 85% of the males and 75% of the females developed lung tumors after 66-68 wk latency period. Hepatocarcinomas developed in 7% of the males and 10% of the females given 0.56 mg hydrazine sulfate daily and in 2 males given 0.28 mg of the compound daily after a latency period of 80 wk; this low incidence was probably due to the long period of latency. These variations in the latency period may indicate that a higher daily intake of the compound for a shorter period has a higher carcinogenic potency than a lower daily intake for a longer period. The occurrence of lung and liver tumors following the administration to mice of hydrazine sulfate in doses corresponding to therapeutic doses of isoniazide administered to man, requires re-evaluation of the role of this drug in human pathology.

- 16 EPIDERMOID CYSTS IN THE THYROID GLANDS OF MALE RATS TREATED NEONATALLY WITH OESTROGEN. (J.) Arai, Y. (Juntendo U. Sch. Med., Tokyo, Japan), Maeda and S. Masuda. *Acta Endocr* 65(1):170-174, 1970.

The incidence of epidermoid cysts in the thyroid gland was determined in intact and castrated (on the day of birth) male rats given estradiol benzoate for 30 successive days from birth (1 µg daily during the first trimester, 2 µg daily during the second, and 1 µg daily during the third, s.c.). The incidence of epidermoid cysts in castrated rats receiving estradiol was 90% but dropped to 30% in intact animals receiving estradiol. No cysts were observed in intact animals given estradiol from days 31-60 after birth or in intact or castrated rats given sesame oil during the first 30 days of life.

- 17 PRODUCTION OF LEUKEMIA AND STOMACH NEOPLASMS IN SWISS, RF, BALB/c AND C3H FEMALE MICE BY FEEDING N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]-ACETAMIDE. (E.) Cohen, S. M. (U. Wisconsin Med. Sch., Madison), E. Ertürk and G. T. Bryan. *Cancer Res* 30(9):2320-2325, 1970.

The survival rate, latent period, and incidence of lymphocytic leukemia and the incidence of stomach neoplasms were determined in Swiss, RF, BALB/c, and C3H female mice fed N-[4-(5-nitro-2-furyl)-2-thiazolyl] acetamide (NFTA). Only 16 Swiss mice fed NFTA (490 mg/mouse/13 wk) in an initial test survived and in gross and microscopic examination 15 had generalized lymphocytic leukemia and 3 had forestomach squamous cell tumors while none of the 51 control mice (surviving 14 to 49 wk) developed leukemia or any other tumors. In a 14 wk dosage study on Swiss mice, a 12 wk latent period for the leukemia was observed at 0.1 and 0.05% dietary levels of NFTA with incidences of 8/9 and 9/13, resp., and an 18 wk latent period was observed at 0.025 and 0.01% dietary levels with incidences of 8/16 and 7/14, resp. Stomach tumors were found in 12/52 mice with 6 of these incidences occurring in the highest dosage range (0.1%). After 14 wk on a 0.1% NFTA diet, leukemia was widespread in RF (12/16), BALB/c (21/29), C3H (12/24), and Swiss (22/22) strains of mice while only 3 controls (all of the RF strain) developed leukemia, and 13 mice fed NFTA displayed stomach tumors while none of the controls were afflicted.

- 0418 CYTOGENIC EFFECT OF CYCLAMATE ON HUMAN PERIPHERAL LYMPHOCYTES *IN VIVO*. (Ger.) Bau-chinger, M. (Radiobiol Inst. U. Munich, Germany), E. Schmid, M. Pieper and N. Zöllner. *Deutsch Med Wschr* 95(44):2220-2223, 1970.

The side effects of the cyclamate sweeteners (sodium or potassium salts of cyclohexylsulfamic acid) were investigated from the point of view of cytogenetic action. A chromosome analysis of peripheral lymphocytes was carried out on: a cyclamate group (3 women, 8 men) who had been placed on a cyclamate regimen due to liver or kidney disease; a control group I (3 women, 7 men) with similar diseases to those of the cyclamate group but on a regimen of fructose; and a control group II (14 women, 38 men) of healthy subjects. Both in the cyclamate group and in control group I, 48-hr cultures were obtained with an analysis of 100 cells; in the control group II 48- and 68-hr cultures were obtained. In the cyclamate group, a mean number of chromosomal aberrations was 3.3% of all evaluated cells, with a mean number of breaks/cell of 0.045, which was about 2 times higher than either control group. The chromosome aberration in the patients with liver disease was not due to a virus infection. However, these changes in the lymphocytes may not be a specific consequence of cyclamate.

- 0419 THE METABOLISM OF CYCLAMATES IN RATS. (E.) Wallace, W. C. (Food Drug Admin., Dept. Hlth. Educ. Welfare, Washington, D.C.), E. J. Lethco and E. A. Brouwer. *Pharmacol Exp Ther* 175(2):325-330, 1970.

Weanling rats of both sexes were fed cyclamates in their diet (0.4, 2.0, or 10%) for a year or more, after which 63 of them were given a p.o. intubation of ¹⁴C-cyclamate (2 µC or 2.2 mg). Essentially all of the administered dose was accounted for in the excreta after 3 days, with 35% appearing in the

urine. The cyclamate was converted to cyclohexylamine in 83% of the rats; amounts ranged from less than 0.1-38%. Small quantities of cyclohexylamine were also found in the feces. No metabolite other than cyclohexylamine was detectable. Although no attempt was made to determine at what stage during the feeding period the conversion of cyclamate to cyclohexylamine took place, prolonged or chronic feeding seemed to potentiate this conversion process. No significant amounts of excreted cyclamates were found in the bile.

- 0420 REPORT ON CYCLAMATES BY THE COMMITTEE SET UP BY THE ISRAEL MINISTRY OF HEALTH. (E.) Berenblum, I. (Weizmann Inst. Sci., Rehovot, Israel). *Israel J Med Sci* 6(4):576-579, 1970.

Artificial sweetening agents, including saccharin and cyclamates, are consumed in Israel primarily in the form of tablets, "low calorie" syrups, and sugarless soft drinks, but their use is not as widespread as it has been in the United States. Studies of the carcinogenic properties of cyclamates in laboratory animals have shown that doses of cyclamates corresponding to a consumption of 3000 tablets/day for humans (2.5 g/kg body wt/day) produced tumors of the urinary bladder in rats; in addition, calcium cyclamate and cyclohexylamine have produced teratogenic effects when injected into chick embryos. Carcinogenic effects have not been demonstrated for cyclamates in man, and the doses which produce tumors in laboratory animals are 50 times the maximum conceivable dose that a man might take. Nevertheless, Israeli authorities have recommended the restriction of the use of cyclamate concentrates and syrups (but not of cyclamate tablets), and they have discouraged the use of any cyclamate-containing product during pregnancy.

- 0421 TUMORIGENICITY OF ALDRIN, DIELDRIN, AND ENDRIN IN THE ALBINO RAT. (E.) Deichmann, W. B. (U. Miami Sch. Med., Fla.), W. E. MacDonald, E. Blum, M. Bevilacqua, J. Radomski, M. Keplinger and M. Balkus. *Industr Med Surg* 39(10):426-434, 1970.

The pesticides aldrin, dieldrin and endrin were fed to weanling rats for the duration of their lives in amounts ranging from 20-50 ppm of aldrin and dieldrin to 2-12 ppm of endrin. The toxic and carcinogenic effects of the agents were observed. Signs of acute toxicity (tremors and convulsions) were noted in a few animals of all experimental groups and were dose-related. The mean life span of females fed the highest levels of aldrin and dieldrin was shortened from a mean of 19.5 months for controls to 13.0 months for females fed aldrin 50 ppm, and 16.6 months for those fed dieldrin 50 ppm. Benign and malignant tumors were observed in 23 tissues or organs in 257 of 793 experimental and in 79 of 163 control rats examined histologically; the highest number of tumors in all groups occurred in mammary and lymphatic tissues. When compared with the controls, male and female rats fed aldrin 20, 30 and 50 ppm, and dieldrin 20, 30 and 50 ppm showed a decrease in the incidence of all tumors

and the decrease was dose-related, being lower in the rats fed the highest doses. No difference was seen in tumor incidence in control rats and experimental rats fed endrin 2, 6 and 12 ppm. The reduction in overall tumor incidence with the pesticides may be due to a disturbance of the normal metabolism of steroid hormones brought about by pesticides' stimulation of hepatic microsomal enzyme activity.

- 0422 PHARMACO-BIOCHEMICAL STUDIES ON CYTOTOXIC POLYOL DERIVATIVES: II. THE EFFECT OF BIOLOGICAL ALKYLATING AGENTS ON THE THERMAL-DENATURATION PROPERTIES OF DNA. (E.) Jeney, A., Jr. (Christie Hosp., Manchester, England), I. Szabo, Valyi-Nagy, L. Institoris and J. Szabo. *Europ J Cancer* 6(9):297-302, 1970.

The effect of biological alkylating agents on the thermal-denaturation profile of DNA (followed spectrophotometrically at 260 mμ) from calf-thymus on nucleohistone was investigated. The melting temperature (T_m) of the DNA control (62.5°C) was decreased by the addition (equivalent concentrations of alkylating agents and DNA) of nitroguanine mustard (52.5°C), Degranol (53.5°C), Merophan (55.0°C), and Endoxan (56.0°C), while dimethylmyleran (63.0°C) did not alter the T_m . The hyperchromic effect of the DNA control (40.0%) was greatly affected by Degranol (38.5%) or nitroguanine mustard (33.5%), although Merophan (26.8%), Endoxan (29.4%), and dimethylmyleran (17.0%) shifted it considerably. Of the cytotoxic hexitols examined (Degranol, dibromodulcitol, dimesylmannitol, dibromomannitol, and dichloromannitol) only Degranol lowered the T_m and none of the derivatives altered the hyperchromic effect. Histone alone raised the T_m of DNA by 10°C, pretreatment with dibromomannitol before histone raised it only slightly and pretreatment with dibromodulcitol or dimethylmyleran before histone completely blocked the increase.

- 0423 INDUCTION OF THYMIC LYMPHOSARCOMA AND MAMMARY ADENOCARCINOMAS IN RATS BY ADMINISTRATION OF THE ANTITUMOR AGENT, 4(5)-(3,3-DIMETHYL-1-TRIAZENO)IMIDAZOLE-5(4)-CARBOXAMIDE. (E.) Skibba, J. L. (U. Wisconsin Med. Sch., Madison, Wis.), Ertürk and G. T. Bryan. *Cancer* 26(5):1000-1004, 1970.

The carcinogenic effects of long-term treatment with the cancer chemotherapeutic agent 4(5)-(3,3-dimethyl-1-triazeno)imidazole-5(4)-carboxamide (DIC) were tested in rats. Twenty-four female weanling rats were fed DIC at a mean cumulative dose of 740 mg/kg body wt/14 wk. The first mammary tumor was palpable 10 wk after the start of feeding DIC, and by the time the experiment was terminated, all 24 rats had developed an average of 5 mammary adenocarcinomas. Lymphosarcoma was present in the thymus of all rats and in the spleen (20/24), lymph nodes (18/24), bone marrow (12/24). Ependymomas of the brain were present in 9 rats and pulmonary alveolar carcinomas in 4 rats. No tumors were found in the contralateral

24 rats. The alkylation of biopolymers, creation of a magnesium deficiency or activation of a latent oncogenic virus were discussed as possible mechanisms of DIC carcinogenesis.

24 INDUCTION OF DELAYED HYPERSENSITIVITY IN GUINEA PIGS BY AFLATOXINS, OTHER COUMARINS AND FURAZOLIUM. (E.) Chung, C. W. (Food, Drug Administration, U.S. Dept. Hlth. Educ. Welfare, Washington, D.C.), A. L. Giles, Jr. and T. R. Carson. *J Invest Dermatol* 55(6):396-403, 1970.

The induction of delayed skin hypersensitivity in guinea pigs by aflatoxins (B_1 , B_2 , G_1 , and G_2) and structurally related compounds was determined and rated according to severity of erythema (fractional response, average intensity, and average of ten times average intensity of positive responses). Animals sensitized intradermally with the lowest amount of aflatoxin B_1 (7.5 μ g) gave at least 1 positive reaction to aflatoxin B_1 challenge at all concentrations (0.10, 0.25, 0.50, and 1.00 μ g), but animals sensitized with larger amounts (30 μ g) by the 1.00 μ g challenge showed a significant sensitization. After immunized animals were challenged repeatedly (2 or more challenges) the initial difference in the degree of sensitization caused by different immunization procedures disappeared. Aflatoxins B_2 , G_1 , and G_2 (10 μ g), coumarin, 8-methoxypsoralen, and furazolium (25 μ g), and sterigmatocystin (20 μ g) were active in causing a delayed hypersensitivity. Animals strongly sensitized by repeated challenges with aflatoxin B_1 showed cross-reactivity to the other aflatoxins, sterigmatocystin, coumarin, and commercial perfumes, and isomers of furocoumarins, while lightly sensitized animals were moderately reactive to the aflatoxins B_2 and G_2 , negatively reactive to sterigmatocystin, and completely unreactive to aflatoxin G_1 . None of the immunized animals showed any circulating antibodies.

25 THE HISTOPATHOLOGICAL EFFECTS OF AFLATOXIN B_1 AND THE PALMOTOXINS B_0 AND G_0 ON THE LIVER OF THE DEVELOPING CHICK EMBRYO. (E.) Bassir, (Dept. Biochem., U. Ibadan, Nigeria) and A. A. Ekunle. *FEBS Letters* 10(3):198-201, 1970.

Chick embryos received inoculations of the palmotoxins B_0 and G_0 , and of the aflatoxin B_1 , (0.3 μ g/g) to determine the hepatic embryotoxic properties of these toxins. Light microscopic examination of the livers of the embryos prepared 21 days after toxin inoculation showed that in livers of embryos inoculated with aflatoxin B_1 lymphocytic infiltration had occurred, and there was a focal area of fatty change. In embryos inoculated with palmotoxin G_0 , there were also peripheral focal areas of fatty vacuolization; focal necroses with mononuclear cellular infiltrations were also observed. In embryos inoculated with palmotoxin B_0 , focal areas of marked periportal necrosis were observed, and severe fatty change had affected the tissue. Fatty infiltration was observed with all toxins inoculated, and the first 2 agents were

more potent inducers of fatty infiltration than the last agent, a finding which suggests that chick embryos are resistant to aflatoxin G_0 .

0426 AFLATOXINS AND LIVER INJURY IN THE RHESUS MONKEY. (E.) Deo, M. G. (All-India Inst. Med. Sci., New Delhi), Y. Dayal and V. Ramalingaswami. *J Pathol* 101(1):47-56, 1970.

The effects of aflatoxins on the livers of rhesus monkeys fed with varying doses of aflatoxins under conditions of good and poor protein nutrition were investigated. Male monkeys were fed with aflatoxin B_1 and G_1 in amounts of 1 mg/kg, 0.25 mg/kg, or 62 μ g/kg at intervals of 1 day, 2 times/wk or once a wk. Animals in the first 2 treatment groups also were divided according to whether they were given a protein-deficient diet or not. Of animals fed on aflatoxin 1 mg/kg and a protein-adequate diet, all died before the end of the third wk of the experiment, and 50% showed extensive hemorrhagic necrosis of the liver; all animals receiving 1 mg/kg which were fed a protein-poor diet also died by the 3rd wk of testing, and, of these, 33% showed liver necrosis. Monkeys fed aflatoxin 0.25 mg/kg developed large bizarre hyperchromatic liver cells and showed bile-duct proliferation; no animals in this treatment group showed hemorrhagic necrosis. By the 15-19th wk of treatment, lesions developed in the livers of both protein-adequate and protein-poor monkeys. Monkeys fed with aflatoxin at 62 μ g showed changes comparable to those observed in the 0.25 mg group, but in a milder form. Changes appeared later in this group, and did not progress significantly during the 2-yr course of the experiment. None of the monkeys developed tumors, and protein deficiency apparently did not exert any clear deleterious influence on the liver injury produced by aflatoxin.

0427 CARCINOGEN-INDUCED TRANSPLACENTAL EFFECTS IN THE RAT: HISTOLOGICAL FINDINGS AND THE KINETICS OF DNA-METABOLISM FOLLOWING THE APPLICATION OF AFLATOXIN B_1 , METHYLAZOXYMETHANOL-ACETATE, AND ETHYLNITROSOUREA. (Ger.) Goerttler, K. (German Cancer Res. Ctr., Heidelberg), H. P. Arnold and D. V. Michalk. *Z Krebsforsch* 74(4):396-411, 1970.

The effects of aflatoxin B_1 , methylazoxymethanol-acetate (MAM) and ethylnitrosourea administration to pregnant rats on DNA synthesis in maternal and fetal livers were investigated. On the 18th day after the insemination of rats, aflatoxin B_1 (1 mg/kg), methylazoxymethanolacetate (10mg/kg) or ethylnitrosourea (50 mg/kg) was injected i.p. Histological examinations of the maternal and fetal livers were made at various times and, 3 H-thymidine incorporation was measured for kinetic activity. Aflatoxin was found to damage the maternal livers but not those of the fetuses, and a 500% and a 200% increase of thymidine incorporation in maternal livers and fetuses, resp., was observed at 48 hr after its administration. MAM caused discrete alterations in the maternal liver and an initial decrease in thymidine incorporation followed by a 130% increase

at 48 hr after its administration; fetal tissues exhibited no morphological alterations and thymidine incorporation was 155% in the head and 120% in trunk tissues at 48 hr after treatment. Ethylnitrosourea caused minor alterations with few hepatocytic necroses in the maternal liver and severe alterations in the cellular layer of the fetal cerebral ventricles and in the olfactory region. A 140% increase in thymidine incorporation was found in maternal livers 24 hr after ethylnitrosourea administration, following an initial drop to 70%, and returned to normal at 48 hr after administration; the fetal head tissues exhibited a 35% decrease of thymidine incorporation at 3 hr and maintained levels of 50-70% 12-24 hr after administration and returned to normal at 48 hr. Thus maternal livers seemed to be more susceptible to aflatoxin B₁ and to MAM than the fetal tissues, while an opposite phenomenon occurred with ethylnitrosourea.

0428 INHIBITION BY AFLATOXIN B₁ OF RAT LIVER ZOXAZOLAMINE HYDROXYLASE INDUCTION. (E.)

Pong, R. S. (Dept. Nutr. Food Sci., Massachusetts Inst. Tech., Cambridge) and G. N. Wogan. *Biochem Pharmacol* 19(10):2808-2812, 1970.

The effect of aflatoxin B₁ on the induction of zoxazolamine hydroxylase activity by 3,4-benzpyrene was investigated. Rats were given a single i.p. injection of 3,4-benzpyrene (10 mg), followed immediately or 3-18 hr later by 3 mg/kg body wt of aflatoxin B₁. Livers were then homogenized and the microsomal enzyme hydroxylase was assayed. Benzpyrene injection caused a 3-fold increase in zoxazolamine hydroxylase activity within 24 hr of injection; a single dose of aflatoxin B₁ completely inhibited enzyme activity when the toxin was administered simultaneously with or 3 hr after the injection of benzpyrene. When aflatoxin B₁ was administered 6 or 12 hr after 3,4-benzpyrene, there was no significant reduction of zoxazolamine hydroxylase for 6 hr thereafter; however at succeeding time periods, a marked decline in enzyme activity was observed. Administration of the toxin at 18 hr after injection of 3,4-benzpyrene had little effect on enzyme activity. The inhibition by aflatoxin B₁ of zoxazolamine hydroxylase activity may have resulted from a suppression of synthesis of new enzyme protein, or from a suppression of activation of a microsomal hydroxylase activity.

0429 ESTABLISHMENT OF A TRANSPLANTABLE ASCITES VARIANT OF A RAT HEPATOMA INDUCED BY 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE. (E.) Smith, D. F. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston), E. F. Walborg, Jr. and J. P. Chang. *Cancer Res* 30(9):2306-2309, 1970.

A transplantable ascites variant, designated ascites hepatoma AS-30D, was established from a 3'-methyl-4-dimethylaminoazobenzene-induced rat hepatoma (0.06% dietary administration over 12 wk) and has been successfully maintained through 75 transplant generations as 2 sublines in male and female rats. The AS-30D tumor cells are of epithelial origin and grow primarily

in clusters (50 x 100 μ). Approximately 90% animals inoculated (10⁸ cells, i.p.) with AS-developed tumors, and the median survival time of host was 14 days.

0430 FINE STRUCTURE OF NUCLEI AS REVEALED BY ELECTRON MICROSCOPY: VII. HYPERPLASTIC NODULES IN RAT INDUCED BY 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE, 2-FLUORENYLACETAMIDE AND DL-ETHIONINE. (E.) Yasuzumi, G. (Nara Med. U., Kashihara, Japan), R. Sugihara, N. Ito, Y. Konishi and Y. Hiasa. *Exp Cell Res* 63(1):83-95, 1970.

The fine structure of the nuclei in hyperplastic nodules developing in livers of rats fed diet containing 3'-methyl-4-dimethylaminoazobenzene, 2-fluorenylacetamide (0.05%), or DL-ethionine for 3 wk was observed by electron microscopy autoradiography. The hepatocyte nuclei within hyperplastic nodules was characterized by a disappearance of the nuclear envelope's inner layer, the disappearance of condensed chromatin aggregates and enlargement of the nucleoli into oval or irregularly-shaped features. No differences in ultrastructural effects of the 3 carcinogens were seen. An electron microscopic autoradiograph indicated that the nucleoli in the hyperplastic area induced by ethionine were synthesizing not as actively as those in the non-treated hepatocyte so that transport of nucleolar product into cytoplasm was blocked, and the turnover of DNA in the hyperplastic nodule was considerably greater than in the non-nodular portions or in normal

0431 STUDIES ON CARCINOGEN-BINDING PROTEIN: I. ISOLATION AND CHARACTERIZATION OF AMINOAZO DYE-BOUND PROTEIN AFTER ADMINISTRATION OF A SINGLE LARGE DOSE OF 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE TO RATS. (E.) Sugimoto, T. (Fac. Sci., Tokyo, Japan) and H. Terayama. *Biochem Biophys Res Commun* 214(3):533-544, 1970.

Male rats received 40 mg of 3'-methyl-4-dimethylaminoazobenzene and were killed after 40 hr; a liver cell sap was prepared and subjected to heat treatment (55°C for 3 min), followed by chromatography on CM-cellulose. Protein-bound dye was located in the nonbasic protein fraction, the slightly basic protein fraction, and the more basic protein fractions (Fractions I, IV, VII and VI, resp.). Subsequent purification procedures, including differential precipitation by (NH₄)₂SO₄ or pH adjustment and finally gel filtration were used to separate several dye-binding proteins, I-a, I-b, VII-a and VII-b. The estimated molecular weights of these dye-binding proteins were 160,000-12,000-15,000, 160,000-170,000, 160,000-170,000, 40,000, resp. Proteins I-a, IV and VII-a showed specific binding of about 1 (mole dye/mole protein) whereas I-b and VII-b showed only a slight binding (0.07 mole dye/mole I-b and 0.01 mole dye/mole VII-b). The isoelectric points of I-a and VII were estimated to be approx. 5.2, 8.0 and 8.0, resp. Polar dye prepared from I-a, a major dye-binding protein under the present experimental

ons, showed mainly P2b and P1 components in addition to P2a, while that prepared from IV or V gave only P2a and P2a'. Preferential binding of Fraction IV protein was demonstrated for non-carcinogenic 2-methyl-4-dimethylaminoazobenzene.

2 THE SYNTHESIS OF MODEL COMPOUNDS FOR THE POLAR DYES DERIVED FROM LIVER OF RATS GIVEN 4-AMINO-2',3-DIMETHYL-AZOBENZENE. (E.) Matsumoto, M. (Inst. Sci. U. Tokyo, Japan) and H. Terayama. *Chem. Interact* 2(1):47-52, 1970.

Synthesis of 2 model compounds (4-(ethylmercapto-1-amino-2',3-dimethylazobenzene and 4-(cysteinyl-1-amino-2',3-dimethylazobenzene) of the carcinogen 4-amino-2',3-dimethylazobenzene (o-AT) was attempted to provide a synthetic approach to investigations of the *in vivo* nitrogen-sulphur bridge between o-AT and rat liver proteins. Presumably, the reaction product of ethyl sulfenyl chloride and o-AT was 4-(ethylmercapto-S-yl)amino-2',3-dimethylazobenzene. N-Trifluoroacetyl-S-thiocyanido-L-cystine methyl ester was obtained from the addition of N-trifluoroacetyl-L-cystine methyl ester to an aqueous solution of lead thiocyanogen and bromine, which was then mixed with o-AT before refluxing in potassium hydroxide/ethanol to produce 4-(cysteinyl-1-amino-2',3-dimethylazobenzene. Both model compounds contained secondary auxochromic amino groups (nitrous acid test), readily liberated o-AT, and exhibited UV and visible spectra similar to the o-AT polar dye formed *in vivo*. Apparently the binding of o-AT and rat liver proteins occurs directly through a nitrogen-sulphur bridge that involves the amino nitrogen of the dye and methionine sulphur.

3 p-DIMETHYLAMINO-AZOBENZENE (DAB) HEPATOCARCINOGENESIS IN RATS: INHIBITION BY TWO NAPHTHYLSISOTHIOCYANATES. (Fr.) Lacassagne, A. (Inst. Med. Paris, France), L. Hurst and M. D. Xuong. *Proc Soc Biol* 164(2):230-233, 1970.

The effect of α - and β -naphthylisothiocyanate (ANIT and BNIT) on p-dimethylaminoazobenzene (DAB) hepatocarcinogenesis was studied in Wistar rats receiving various compounds added to their usual (low protein and low riboflavin) diet. Six groups of animals were treated as follows: ANIT only (1 g/kg food, 8 rats), BNIT only (1 g/kg food, 10 rats), ANIT and DAB (0.6 g/kg food, 16 rats), BNIT and DAB (0.6 g/kg food, 16 rats), ANIT only (0.5 g/kg food, 10 rats) or ANIT and DAB (0.5 g/kg food) and DAB (0.6 g/kg food, 12 rats). All animals were autopsied between 50 and 480 days. ANIT alone or associated with DAB produced considerable enlargement of the portal vascular network and multiple ramifications of the peribiliary bile ducts, which developed earlier than in case of DAB administration. However, no lobular infiltration with malignant cells (occurring 25 days after DAB treatment, first stage) was noticed; slight granulosity of the peripheral liver was observed in 1 animal at day 41 after treatment with DAB. Later stages of progressive malignancy started to occur after 99 days of treatment. BNIT caused dilatation of the portal network with no bile duct involvement; it inhibited com-

pletely the effect of DAB in animals subjected to both BNIT and DAB; no alterations specific to hepatic oncogenesis occurred.

0434 REDUCTION OF THE NUMBER OF ANTIGENS IN RAT LIVER TISSUE IN THE PROCESS OF HEPATOCARCINOGENESIS. (Rus.) Khundanova, L. L. (USSR Minist. Publ. Hlth., Leningrad). *Vop Onkol* 16(8):52-57, 1970.

The reduction of the number of rat liver tissue antigens in the process of dimethylaminoazobenzene (10 mg in diet for 300-330 days) hepatocarcinogenesis was studied in male rats with antisera from immunized chinchilla rabbits and compared to liver antigens of animals treated with noncarcinogenic diethylaminoazobenzene (10 mg in the diet for 100 days). The loss of 2 normal liver antigens of the α_2 - and β -globulin region was noticed in the diethylaminoazobenzene-treated animals on the 4th day of the experiment; such loss occurred on the 15-30th days in some and on the 60-100th in most of the livers of carcinogen-treated animals; no loss of liver antigens was noticed on the 400th day of the experiment. Two antigens were missing from the hepatoma cells: one from the albumin or α_1 -globulin and the other from the α_2 - or β -globulin regions. The loss of similar (non-organ specific) antigens from liver proteins in both carcinogen- and analogue-treated animals indicated that this loss was due to a hepatotoxic effect exhibited by both compounds, while the absence of the α_1 -globulin antigen from the hepatomatous tissue seemed to be specific for the carcinogenic process.

0435 EXPERIMENTAL INVESTIGATIONS IN "SYNCARCINOGENESIS": VI. ADDITION OF MINIMUM DOSES OF FOUR DIFFERENT LIVER CARCINOGENS IN RATS IN LIVER CANCER DEVELOPMENT. (Ger.) Schmäh, D. (German Cancer Res. Ctr., Heidelberg). *Z Krebsforsch* 74(4):457-466, 1970.

An investigation was carried out to determine if syncarcinogenesis occurs when several carcinogens of various structures but with similar organotropy are administered in doses that are below tumor formation level when each is administered by itself. Ninety-six rats were given 4-dimethylaminoazobenzene (3mg/kg), dimethylnitrosamine (0.01 mg/kg) diethylnitrosamine (0.05 mg/kg) and nitrosomorpholine (0.2 mg/kg) daily p.o. for 580 days in subthreshold doses. The rats tolerated the carcinogens as well as 100 control animals, surviving for 760 days \pm 110 days; the weight gain in the experimental animals exceeded that of the control rats. The first hepatocellular carcinoma appeared after 520 days and of the original 96 animals, 86 were still alive at that time. Of these, 29 (34%) developed malignant liver tumors, 20 with hepatocellular carcinoma and 9 with hemangioendothelioma, particularly sarcoma of the liver. Metastases were observed in 6 of the 29 rats. No tumors developed in the control animals.

- 0436 BLASTOMOGENIC EFFECT OF POLYCYCLIC HYDROCARBONS: AGE DEPENDENCE OF THE EXPERIMENTAL ANIMALS. (Rus.) Bolonina, N. I. (P. A. Herzen Res. Inst. Oncol., Moscow, USSR). *Vop Oncol* 16(6): 73-76, 1970.

The age-dependent susceptibility to polycyclic hydrocarbons carcinogenicity was studied in August and Wistar rats and in C3HA and C57BL mice on 2-3 wk-old and 6 months-old animal groups of both sexes. Each animal received 0.5 mg of 7,12-dimethylbenz(a)anthracene (DMBA dissolved in paraffin, s.c.) or 0.125 mg of 3-methylcholanthrene (dissolved in apricot oil). Tumors developed in 40-56% of the animals of the younger animals, and in 68-87% of the older animals, after a latency period of approximately 3.8 months. The latency period in the baby mice (3.5 months) was 1 month shorter than in the adult mice (4.5 months). No interspecies differences in carcinogen susceptibility were noticed; marked differences were observed, however, within the species. The incidence of induced tumors was 56% (younger animals) and 87% (older animals) in the August rats and 40% and 68%, resp., in the Wistar rats. Tumor incidence was 42.5% in C57BL baby mice and 54.7% in C3HA baby mice with no differences in incidence in the adult mice. Myoblastic sarcomas (with a considerable degree of differentiation) were prevalent (40%) among the induced tumors of the younger animals while polymorphic cell sarcomas predominated in the older animals. The adult animals seemed to be more susceptible to polycyclic hydrocarbon carcinogenesis, possibly due to age-determined differences in the rate of carcinogen excretion.

- 0437 SUSCEPTIBILITY OF GUINEA PIGS TO CHEMICAL CARCINOGENS: 7,12-DIMETHYLBENZ(a)ANTHRACENE AND URETHAN. (E.) Toth, B. (U. Nebraska Coll. Med., Omaha) *Cancer Res* 30(10):2583-2589, 1970.

Guinea pigs (average wt of 94 g) received a single s.c. injection of 7,12-dimethylbenz(a)anthracene (DMBA) at birth (in amounts of 0.1-50 mg) or 3 i.v. injections of DMBA (3 mg every 3rd day for 3 doses) or urethan (1 mg/g body wt every 3rd day for 5 doses, s.c.) or 0.5 ml tri-*n*-caprylin (the base used for the DMBA and urethan) as control. The incidence, site, and histological type of induced tumors were observed, and the relative susceptibility of guinea pigs to tumor development following DMBA and urethan treatment was assessed. Following s.c. DMBA treatment, 33 animals developed a total of 37 s.c. tumors at the injection site, of which 16 were fibrosarcomas. In addition, malignant lymphomas, tumors of skin, lungs, uterus, ovaries, breast, etc., were also caused by the treatment. The i.v. injections of DMBA gave rise to higher incidences of tumors of the breast, lungs, uterus, ovaries, and skin than in the corresponding control groups. Five s.c. injections of urethan produced tumors of lungs and ovaries. The findings indicate that the guinea pig is at least as susceptible as the mouse to tumor induction by DMBA and urethan.

- 0438 EFFECT OF VARIOUS STEROIDS ON THE ADRENAL NECROSIS INDUCED BY 7,12-DIMETHYLBENZ(a)ANTHRACENE IN RATS. (E.) Somogyi, A. (Inst. Exp. Surg., U. Montreal, Quebec, Canada) and Kovacs. *Rev Canad Biol* 29(2):169-180, 1970.

The effects of various steroids with diverse properties on the action of 7,12-dimethylbenz(a)anthracene (DMBA) on the adrenal of the rat were determined by gross and histological observations. Spironolactone (18 mg, p.o.) completely inhibited the adrenocorticolytic effect of DMBA (40 mg, i.v.), while ethylestrenol (12.5 mg, p.o.), inhibited the effect by 50% (mortality studies indicated that spironolactone counteracted the general toxicity of DMBA). Testosterone (12.5 mg, p.o.) and corticosterone (17.5 mg, p.o.) moderately aggravated the DMBA-induced (3 mg, i.v.) adrenal necrosis (30% incidence in controls rose to 80%), and estradiol (1 mg, p.o.) and methylandrostenediol (13.2 mg, p.o.) exerted a very strong effect (100% incidence). Estradiol aggravated the DMBA-induced lesions at concentrations of 100 µg - 10 mg, while methylandrostenediol caused the aggravation only at concentrations of 5-10 mg. Hypophysectomy performed before initiation of estradiol treatment only slightly decreased the intensity of adrenal and ovarian grafts in the spleen did not affect the incidence or severity of lesions. Injections of the DMBA-metabolite 7-hydroxymethyl-12-methylbenz(a)anthracene (1.5 mg, i.v.) failed to produce adrenal necrosis, but animals which were treated with estradiol before the metabolite was administered developed severe bilateral adrenocorticolysis. Progesterone (13.6 mg), norbolethone (13.7 mg), ethylestrenol (12.5 mg), triamcinolone (17.0 mg), desoxycorticosterone (16.1 mg) neither inhibited nor aggravated DMBA-induced adrenal necrosis.

- 0439 GENETIC DELETIONS AT SPECIFIC LOCI IN POLYCYCLIC HYDROCARBONS IN RELATION TO CARCINOGENESIS. (E.) Fahmy, O. G. (Inst. Cancer Res., Roy. Cancer Hosp., London, England) and Fahmy. *Int J Cancer* 6(2):250-260, 1970.

The specific mutagenicity (classical technique outlined by Fahmy and Fahmy) of 4-dimethylbenz(a)anthracene with markedly different carcinogenic activities (7,12-dimethylbenz(a)anthracene, 7-bromomethylbenz(a)anthracene, 1,7-dimethylbenz(a)anthracene, and 3,9-dimethylbenz(a)anthracene) was tested in *Drosophila melanogaster*. All of the compounds proved inactive in the induction of sex-linked autosomal recessive (visible and lethal) point mutations; where marginal activity was observed, it could not be correlated with carcinogenesis. The highest incidence occurred in the non-carcinogenic 3,9-dimethylbenz(a)anthracene. Biochemical demonstrable DNA deletions within the nucleolar organizer region in the major heterochromatic region of the X-chromosome results in *bobbed* mutations and both the carcinogenic agents 7,12-dimethylbenz(a)anthracene and 7-bromomethyl-12-methylbenz(a)anthracene induced a high frequency of

mutations (6.6 per 1000 and 2.2 per 1000, resp.) compared to the controls (0.7 per 1000). These agents were similarly reactive on the *Minute* loci (4.0 and 6.1 per 1000, resp.) although all the compounds proved inactive on euchromatin loci of the X-chromosome. The mutagenicity of carcinogenic material appears to be specific for loci, chemical structure of the carcinogen, and the metabolic activity of the target cells.

0440 SUPPRESSION BY ERGOCORNINE AND IPRONIAZID OF CARCINOGEN-INDUCED MAMMARY TUMORS IN RATS: EFFECTS ON SERUM AND PITUITARY PROLACTIN LEVELS. (E.) Nagasawa, H. (Natl. Cancer Inst., Tokyo, Japan) and J. Meites. *Proc Soc Exp Biol Med* 35(2):469-472, 1970.

The effect of ergocornine, iproniazid phosphate, or dopamine (0.6 mg, 7.5 mg and 0.1 mg, resp., daily for 15-25 days) on tumor enlargement was studied. Female rats were given 5 mg of 7,12-dimethylbenz(a)anthracene i.v., and when the ensuing mammary tumors attained 1 cm in size, injection of the 3 drugs was initiated. Although dopamine had no appreciable effect on tumor growth, iproniazid phosphate and ergocornine injections completely suppressed tumor growth. A 2-fold increase in number of tumors developed was observed after drug injections were begun in dopamine-treated and control rats, whereas no significant change in number of tumors was observed in rats receiving either of the other 2 drugs. Rats treated with ergocornine had significantly lower serum and pituitary concentrations of prolactin (27.8 ng/ml of serum) than did animals treated with the other drugs (concentrations of 109.6 and 85.4 ng/ml serum for iproniazid and dopamine, resp.) Although the mechanism of mammary tumor growth inhibition by iproniazid is obscure, ergocornine probably acts by inhibiting the secretion of pituitary prolactin.

0441 THE EFFECT OF INCREASED NUMBERS OF CARCINOGENIC TREATMENTS ON THE INDUCTION OF CERVICO-VAGINAL AND VULVAL TUMOURS IN INTACT AND CASTRATE RATS. (E.) Glucksmann, A. (Strangeways Res. Lab., Cambridge, England), and C. P. Cherry. *Brit J Cancer* 24(2):333-351, 1970.

Induction of cervico-vaginal (epithelial and sarcomatous) and vulval tumors by 5, 10, 20 or 40 weekly local applications (swabbing the cervix, vagina and introitus) of 7,12-dimethylbenz(a)anthracene (DMBA, 1% solution in acetone) was studied in intact and castrated rats. Histologically, epithelial tumors progressed from a hyperplastic lesion with radiation to extruding or intruding papillomas and to fully developed autonomous carcinomas, but sarcomas formed rapidly and the early stages were not detected. The threshold for induction of cervical-vaginal epithelial tumors was less than 5 weekly paintings and the incidence rose to 60% for castrates and 20% for intact after 10 and 20 weekly paintings before dropping off to 10-15% for both groups after 40 paintings. Castration increased the incidence of vulval

tumors at the lower dose levels (5 and 10 weekly paintings) so that 50% of the epithelial tumors in castrates were carcinomas compared to 20% in the intact animals. The incidence of cervico-vaginal sarcomas leveled off in castrate animals (to approximately 30%) after 20 paintings but increased drastically in intact animals after 20 and 40 paintings (to 20% and 70%, resp.).

0442 THE PRODUCTION OF MAMMARY CARCINOMAS IN RATS BY 9,10-DIMETHYL-1,2-BENZANTHRACENE AND ITS RELATIONSHIP TO THE OESTROUS CYCLE. (E.) Young, S. (Imperial Cancer Res. Fund, London, England), D. M. Cowan and C. Davidson. *Brit J Cancer* 24(2):328-332, 1970.

The influence of the estrous cycle on the induction of mammary carcinoma by 7,12-dimethylbenz(a)anthracene (DMBA, 30 mg, p.o.) was investigated in Sprague-Dawley rats. The percentage of rats which developed mammary adenocarcinomas was similar in all phases of the cycle (81.4%, 76.2%, 73.5%, and 73.4%). However, the actual total number of tumors observed was significantly higher for the animals receiving DMBA during the di-estrous cycle (350 tumors in 57 rats) compared to the pro-estrous (205 in 48 animals), estrous (132 in 36 animals), and met-estrous (278 in 58 animals) cycles. The number of carcinomas produced by different groups of animals in the same phase of the estrous cycle also differed significantly, but the induction period of carcinomas was not affected by the stage of the cycle (12.5 to 13.5 weeks).

0443 A STUDY OF EARLY EPIDERMAL CARCINOGENESIS RELATED TO STAGES OF THE HAIR FOLLICLE CYCLE. (Rus.) Garibyan, D. K. H. (Armenian Inst. Roentgenol & Oncol, USSR) and S. A. Papoyan. *Zh Eksp Klin Med* 10(2):56-61, 1970.

The dynamics of early carcinogenesis was observed on white 2-3 month-old mice treated with 7,12-dimethylbenz(a)anthracene (0.5% soln in benzene, topically applied to the intercostal epidermis one time) during the growth and rest stages of the hair follicle cycle. The carcinogen was applied in the growth stage 3 days or in the rest stage 25 days after hair plucking. Temporary epidermal hyperplasia and enlargement of epithelial cell nuclei was noticed 24 hr following carcinogen application in the growth stage; this hyperplasia decreased in favor of epidermal keratinization during the subsequent days while hair follicle growth continued as in the controls. The carcinogen applied during the rest stage produced necrotic areas with hyperplastic boundaries on the epidermis and inflammation of the dermal skin layers; the sebaceous glands appeared enlarged and the follicle entered the catagen stage at the 30th day. The hair follicle cycle stages had a definite impact on the development of skin alterations during the early stages of carcinogenesis. The lower incidence of tumors produced by the carcinogen when applied during the follicle growth stage was possibly related to a lower oncogenic skin susceptibility during this stage.

- 0444 HAMSTER DEPIGMENTATION PRODUCED BY ORAL ADMINISTRATION OF 9,10-DIMETHYL-1,2-BENZ-ANTHRACENE. ROLE OF EPIPHYSECTOMY. (Fr.) Aubert, C. (Inst. Gustave-Roussy, Val-de-Marne, France) and C. Bohuon. *C R Acad Sci* 271(2):281-284, 1970.

Single doses of 7,12-dimethylbenz(a)anthracene (DMBA) in labrafil were administered p.o. to 4 hamster groups: 65 animals received 1 mg/3 g, 37 received 1 mg/4 g, 40 received 1 mg/5 g and 31 received 1 mg/8 g body wt. One group (27 animals) received benzanthrane (1 mg/3 g body wt) instead of DMBA, and the control group received only labrafil. Several animals were epiphysectomized before or after DMBA administration. Early depigmentation occurred 1 month after DMBA treatment in animals receiving high doses; these doses were larger than the amount necessary for induction of melanoma. Depigmentation persisted throughout the life of the animals, differed with sex and was not transmissible to descendants. Benzanthrane and labrafil had no depigmentation effects. Epiphysectomy performed 48 hr before or after DMBA administration had no effect on the depigmentation response, which seemed to exclude any endocrine involvement. The depigmentation response to high doses of DMBA seemed to be related to its toxicity and not to the carcinogenic effects produced by much lower doses (1 mg/20 g body wt).

- 0445 DIMETHYLBENZANTHRACENE TUMORIGENESIS AND ARYL HYDROCARBON HYDROXYLASE IN MOUSE SKIN: INHIBITION BY 7,8-BENZOFLAVONE. (E.) Gelboin, H. V. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), F. Wiebel and L. Diamond. *Science* 170(3954):169-171, 1970.

The importance of the mouse skin aryl hydrocarbon hydroxylase enzyme system in converting carcinogens (7,12-dimethylbenz(a)anthracene) to toxic forms was studied. When added to enzyme preparations (from control mice or mice in which the enzyme was previously induced with 1,2-benz(a)anthracene) in concentrations equimolar with the substrate, 7,8-benzoflavone and 5,6-benzoflavone inhibited the hydroxylase activity by 77-91%, while 1,2-benzanthracene was relatively inactive (21-27% inhibition); *in vivo* topical application of the flavones, 1,2-benz(a)anthracene, or 7,12-dimethylbenz(a)anthracene (DMBA) produced an induction of the hydroxylase system. Single small doses of DMBA (25 µg, topical application) followed by a promoting agent (croton oil) or repeated doses of DMBA (20 µg, topical application) initiated tumorigenesis, but 7,8-benzoflavone (21.2-27 µg, topical application) inhibited papilloma formation by 39-90%. 7,8-Benzoflavone is effective in inhibiting both aryl hydrocarbon hydroxylase in skin and DMBA-induced tumor, suggesting that this enzyme may be responsible for converting DMBA to the active carcinogenic form.

- 0446 THE REFRACTORINESS OF THE SKIN OF HAIRLESS MICE TO CHEMICAL CARCINOGENESIS. (E.) Giovannella, B. C. (Stehlin Found., Houston, Texas), J. Liegel and C. Heidelberger. *Cancer Res* 30(10):2590-2597, 1970.

Adult and newborn hairless and haired mice of the strain received topical treatment with 7,12-dimethylbenz(a)anthracene in amounts of 100 µg/0.1 ml distilled acetone; the aim was to investigate the difference in susceptibility of hairless and hairy mice to tumor induction by this carcinogen. After more than 10 wk, 44 hairless mice had developed only 7 papillomas, while 87 papillomas and 3 carcinomas had appeared in their 13 haired siblings, and 127 papillomas and 9 carcinomas had developed in 69 Swiss haired mice. Thus, the skin of haired mice was much more susceptible to chemical carcinogenesis than the skin of hairless mice. Injury to the skin with needles with or without promotion with croton oil did not alter these results. Newborn "haired" and "hairless" mice have equal amounts of hair during the first 2 weeks of life; when treated in the above manner during this period "hairless" mice developed 34 papillomas and 3 carcinomas, while 70 "haired" mice developed 66 papillomas and 11 carcinomas. Apparently, the hair follicle and its appendages play an important role in the process of cutaneous chemical carcinogenesis in mice.

- 0447 ON THE BIOCHEMICAL MECHANISM OF TUMOR GENESIS IN MOUSE SKIN: III. DECREASE IN TUMOR YIELDS BY POLY I/C ADMINISTERED DURING INITIATION OF SKIN BY AN INTRAGASTRIC DOSE OF 7,12-DIMETHYLBENZ(a)ANTHRACENE. (E.) Kreibich, G. (German Cancer Res. Ctr., Heidelberg, Germany), R. V. Kinzel and E. Hecker. *Z Krebsforsch* 74(4):389, 1970.

Tumor incidence and average tumor yield were determined in mice with skin tumors induced by intragastric application of 7,12-dimethylbenz(a)anthracene (10 µmoles) followed by the topical application of 12-O-tetradecanoyl-phorbol-13-acetate (TPA, 0.1 µmoles twice weekly for 24 wk; the synthetic double-stranded polyinosinic acid/polycytidylic acid (polyI/C) was administered (100 µg, i.p.) at initiation and before and during promotion. Animals given polyI/C during initiation showed a 2-week delay in the development of tumors, and the average yield was significantly reduced more than 50% compared to control animals. Animals receiving polyI/C before promotion had tumor incidence and average yields comparable to control animals, while animals receiving the polyI/C during promotion showed a slight decrease in tumor incidence (20%) with a slight increase in average tumor yield (10-20%).

- 0448 THE EFFECT OF TESTOSTERONE TREATMENT ON THE UPTAKE OF ³H-OESTRADIOL-17β BY 7,12-DIMETHYLBENZANTHRACENE-INDUCED RAT MAMMARY TUMORS. (E.) Mobbs, B. G. (Dept. Urol., Queen's U., Kingston, Ontario, Canada). *J Endocr* 48(2):293-297, 1970.

The effect of testosterone treatment on the uptake of 6,7-³H-estradiol in dimethylbenzanthracene-induced mammary tumors in rats was investigated. Female rats were given 20 mg of dimethylbenzanthracene

anthracene via gastric instillation, and when mammary adenocarcinomas had begun to develop the animals were treated with repeated s.c. injections of testosterone (0.2 or 1.0 mg) or with s.c. implants of 60 mg pellets of testosterone. After 10-39 days, rats were injected with 16.7 μ C of 6,7-³H-estradiol, with or without auxiliary testosterone injections. Testosterone implantation and injection of testosterone in amounts of 1 mg daily produced regression in 6 of 15 tumors. Pretreatment with testosterone lowered the uptake of 6,7-³H-estradiol, but the results were not statistically significant; however, it seemed clear that the uptake was lower when the amount of testosterone injected was high. Prolonged treatment with testosterone may alter the concentration of estradiol in the tumor tissue by affecting the metabolism of estradiol.

0449 THE EFFECT OF TESTOSTERONE ON CHEMICAL CARCINOGENESIS IN THE BUCCAL POUCHES OF CASTRATED AND INTACT MALE HAMSTERS. (E.) Polliack, A. (Rothschild-Hadassah U. Hosp., Jerusalem, Israel), I. Charuzy and I. S. Levij. *Path Microbiol* 35(5):348-354, 1970.

The effect of testosterone injections on carcinogenesis by 7,12-dimethylbenz(a)anthracene in castrated and intact hamsters was investigated. Twenty-four hamsters were castrated and 24 left intact, and both groups were given topical applications of DMBA on the cheek pouches (0.5% soln); test animals also received i.m. injections of 1.5 mg of testosterone propionate. After 9 and 12 wk of treatment, the number of squamous cell carcinomas in intact animals receiving both DMBA and testosterone was less than 50% that in animals receiving DMBA alone. Among castrated animals at 9 wk, the number of squamous cell carcinomas in animals treated with both DMBA and testosterone was compared to 3 in animals receiving DMBA alone; however at 12 wk, both groups had a similar incidence of the tumors. The tumor incidence in intact and castrated hamsters receiving DMBA alone was comparable throughout the experiment.

0450 EFFECT OF INSULIN AND OF ALLOXAN DIABETES ON GROWTH OF THE RAT MAMMARY CARCINOMA *IN VIVO*. (E.) Heuson, J. C. (Inst. Jules Bordet, Brussels, Belgium) and N. Legros. *Europ J Cancer* (9):349-351, 1970.

The effect of insulin and of alloxan diabetes on the growth of dimethylbenzanthracene-induced rat mammary carcinoma *in vivo* was determined. Animals receiving insulin (2.5 U/100 g, s.c.) and 10% glucose beverage exhibited rapid tumor growth over the 6 week observation period (10.2 cm²), and animals receiving either insulin or glucose exhibited tumor growth less rapid than the first group (6.1 and 2.5 cm², resp.) but significantly higher than controls (1.6 cm²). Diabetes (alloxan-induced 146 days after DMBA) caused regression of 57 tumors (90%) present at the onset of the study, and the tumors that remained unchanged or that continued to grow were found to be insulin-

independent when tested in organ culture. The growth-regulating effect of insulin appears to be a direct action of insulin on the tumors *in vivo*.

0451 9,10-DIMETHYL-1,2-BENZANTHRACENE CARCINOGENESIS IN THE HAMSTER CHEEK POUCH: INHIBITORY EFFECT OF TOPICALLY ADMINISTERED CORTISONE ACETATE. (E.) Polliack, A. (Hadassah U. Hosp., Jerusalem, Israel), I. S. Levij and J. W. Rwmushana. *Arch Path* 90(6):494-498, 1970.

Solutions of 7,12-dimethylbenz(a)anthracene (DMBA) (0.5% soln) and cortisone acetate (0.05% soln) were painted on the cheek pouches of hamsters 3 times/wk for 12 weeks; control animals were treated with DMBA or cortisone or paraffin. The average yield of carcinomas in treated cheek pouches was 0.6 for the DMBA and cortisone treatment; after treatment with DMBA only, it was 3.0. Decrease of tumor formation after cortisone was probably due to depression of DNA synthesis and mitotic activity by the hormone. Cortisone stabilizes biological membranes; its action on cell multiplication may be related to decreased membrane permeability with consequent inhibition of release of lysosomal enzymes which play a part in early stages of cell division. No epithelial changes were found in paraffin-treated animals, while slight hyperkeratosis of the pouch epithelium was occasionally noted in cortisone-treated animals.

0452 INHIBITION OF CHEMICAL CARCINOGENESIS IN THE HAMSTER CHEEK POUCH BY TOPICAL CHLORPROMAZINE. (E.) Levij, I. S. (Rothschild-Hadassah U. Hosp., Jerusalem, Israel) and A. Polliack. *Nature* 228(5276):1096-1097, 1970.

The effect on chemical carcinogenesis of the membrane-labilizing agent chlorpromazine was investigated. The carcinogen 7,12-dimethylbenz(a)anthracene was applied topically to the cheek pouches of hamsters (0.5% concentration) alone or together with chlorpromazine (1.2% concentration). Although the hamsters treated with carcinogen and chlorpromazine showed mild benign epithelial hyperplasia, the development of epithelial neoplasia was significantly suppressed in this group. Nine wk after treatment 4 of the hamsters treated with carcinogen alone had developed atypical papillomas, while none of those treated with carcinogen and chlorpromazine had developed tumors; after 12 wk 6/6 of the animals treated with carcinogen alone and 1/6 of the animals treated with carcinogen and chlorpromazine had papillomas. The inhibitory effect of chlorpromazine on chemical carcinogenesis may have been due to decreased permeability of cell membranes brought about by chlorpromazine.

0453 EXPERIMENTAL LIP CANCER IN HAMSTERS. (Rus.) Zil'fyan, V. H. (Inst. Roentgenol. and Oncol. Armenian S.S.R. Minist. Publ. Hlth., Erevan, USSR), B. S. Fichidzhyan and V. A. Kumkumadzhyan. *Vop Onkol* 16(6):66-69, 1970.

Cancer formation in the lip mucosa was studied in 33 grey Armenian hamsters, 80 white mice and 40 white rats. The inferior lip mucosa was treated topically with 7,12-dimethylbenz(a)anthracene (DMBA as a 0.08% benzene soln on alternate days for 4 months, a total of 60 applications). Most hamsters exhibited dryness and bleeding fissures of the inferior lip mucosa 20 days after the start of the treatment. Hair loss in the chin region (exposed to traces of DMBA) occurred at 2.5-3 months and the first papillomas of the inferior lip mucosa (in 23 hamsters) appeared at 3.5 months of the experiment; lip mucosal cancer developed 1 month later (in 16 of the 23 hamsters with papilloma). The hamsters with lip cancer died at 5.5 months-1 yr after the beginning of the treatment. Most of the white mice presented a thickening of the inferior lip and regional hair loss during the 2nd wk of treatment; ulcerations of the inferior lip mucosa and papillomas in the chin region appeared at 3 months of treatment; no malignancy was noticed among the 20 surviving mice at 5 months of the experiment. The 37 surviving white rats exhibited no alterations of the lip mucosa. Grey hamsters seemed to be more resistant to DMBA toxicity than mice and more appropriate for studies in experimental carcinogenesis.

0454 THE EFFECT OF TUMOUR GROWTH ON IMMUNE COMPETENCE: A STUDY OF DMBA MAMMARY CARCINOGENESIS IN THE RAT. (E.) Kearney, R. (Roy. Brisbane Hosp., Australia) and L. E. Hughes. *Brit J Cancer* 24(2):319-327, 1970.

The 7S and 19S antibody response (modified method of Nossal) to flagella (from motile *Salmonella adelaide*) was followed during the development of 7,12-dimethylbenzanthracene (DMBA)-induced (intragastric instillation of 4 weekly 10 mg doses) mammary carcinoma in Sprague-Dawley rats to determine if immune depression gives rise to tumors or if it is an effect of tumors in these animals. Both primary and secondary responses were depressed in female rats fed the carcinogen compared to controls ($p < .01$ at 16 weeks); surgical removal of the tumors in the carcinogen-fed animals did not restore the response. Both the 19S and 7S antibodies were equally reduced in the DMBA-treated group. Mamectomy performed after the feeding with carcinogen failed to prevent tumor development, correlating with the continued antibody depression observed in these animals. Male rats fed DMBA did not develop malignant tumors or exhibit the antibody depression, suggesting that the tumor development was involved in the depression of immune response.

0455 IMMUNIZATION OF RATS WITH A HETEROGENOUS COMPLEX: THE EFFECT ON THE GROWTH AND METASTASIS OF INDUCED TUMORS. (Rus.) Lomakin, M. S. (Acad. Med. Sci. USSR, Moscow) and E. V. Sokolova. *Biull Eksp Biol Med* 70(9):69-72, 1970.

Muscle sarcomas were induced in 110 Wistar rats, 6-8 months-old, by administration of 7,12-dimethylbenz(a)anthracene (DMBA, 5 mg in vaseline oil,

single dose). The major part of each tumor was surgically removed 4 months after DMBA administration, and the rats were distributed into 5 groups: 1) the experimental group (24 animals) subjected to immunization with a mixture of autologous tumor cells combined with human serum γ -globulin, diazobenzidine and Freund adjuvant (1.5 ml total mixture given twice at 12 days intervals); 2) control group I (22 animals) treated only with autologous tumor cells; 3) control group II (14 animals) treated with diazobenzidine and human serum γ -globulin; 4) control group III (25 animals) with their tumors removed and 5) control group IV (14 animals) tumor-bearing rats subjected to no treatment. All animals were sacrificed 40 days after last immunization. Recurrent tumors revealing lymphoid infiltration and cell necrosis developed in 14 rats and metastases appeared in 4 animals in the experimental group; 19 animals developed tumors and 12 had metastases in control group I; 12 rats had tumors and 8 had metastases in control group II; all animals developed tumors in control groups III and IV, and 14 and 13 rats developed metastases respectively. A single precipitin band (agar) of sera from all animals with autologous tumor tissue antigens was noticed in 62% of the experimental group, in 20% of control group I, in 15% of control group II and in 1% of control groups III and IV. Apparently, immunization with autologous tumor cells combined with exogenous protein produced an activation of humoral and cellular immunity factors which inhibited both growth and metastases of the primary and induced tumors.

0456 EFFECTS OF ANTI-LYMPHOCYTE SERUM ON THE GROWTH OF URIDINE BY LYMPH NODES DURING CARCINOGENESIS. (E.) Woods, D. A. (Imperial Cancer Research Fund., London, England) and C. M. Heath. *Nature* 228(5267):169-170, 1970.

The effect of anti-lymphocyte serum on the uptake of uridine by the lymph nodes during carcinogenesis was investigated in hamsters. The cheek pouch of 28 hamsters were painted with 0.5% dimethylbenzanthracene in mineral oil; 16 of the animals received anti-lymphocyte serum with a cytotoxic titer in excess of 256. Autoradiographic studies of tissues of hamsters which had received i.p. 10 μ Ci of 3 H-uridine showed the paracortical region of the nodes of all tissues examined to contain many pyroninophilic cells, some of which were uridine labeled. Hamsters treated with dimethylbenzanthracene and anti-lymphocyte serum for 3 wk showed the highest counts of pyroninophilic cells (mean cell counts/unit area: 3 and 5, resp.), while hamsters treated with dimethylbenzanthracene for 12 wk, and those treated with anti-lymphocyte serum and dimethylbenzanthracene for 12 wk showed the highest counts of pyroninophilic cells (mean cell counts/unit area: 24 and 10, resp.). In electron microscope autoradiographs the labeled cells resembled lymphocytes. Lymph node hypertrophy was most pronounced in animals treated with dimethylbenzanthracene. Impairment of the cell mediated immune response and blast cell activity by anti-lymphocyte serum, as evidenced by the relatively

bers of cells able to incorporate large quantities of uridine, may be related to the enhancement of pouch tumors.

0457 INDUCED-MAMMARY GLAND TUMORS IN RATS:
TESTING OF ANTITUMOR AGENTS. (Rus.)

Beskovny, A. M. (Inst. Endocr. Hormone Chem., Kharkov, USSR). *Vop Onkol* 16(8):62-66, 1970.

A model for cancer induction and treatment was developed in female Wistar rats 55-65 days-old administered 7,12-dimethylbenz(a)anthracene (10 mg in 0.5 ml olive oil, p.o. 3 times at 10-12 day intervals). Mammary gland tumors developed in 85-90% of the experimental animals after an average latency period of 36 days. Spontaneous regression of tumors occurred in 30% of the animals at the stage when their conventional volume was around 1000 mm³. Irreversible tumor growth occurred when its conventional volume became approximately 4000 mm³ (29 days after the first detection of the tumor by palpation). At this stage 80% of the tumors revealed an adenocarcinomatous structure, and testing of antitumor preparations was started on castrated and nonovariectomized animals. The response to therapeutic agents of DMBA-induced mammary gland carcinoma in rats was established as a valid model for such studies in human breast carcinoma.

0458 THE ROLE OF MICROSOMAL DRUG-METABOLIZING
ENZYMES IN THE BILIARY EXCRETION OF 3,4-
BENZPYRENE IN THE RAT. (E.) Levine, W. G. (Albert
Einstein Coll. Med., Yeshiva U., Bronx, N.Y.).
J Pharmacol Exp Ther 175(2):301-310, 1970.

The biliary excretion of the metabolites of the carcinogen 3,4-benzpyrene was investigated, with special reference to the role of microsomal drug-metabolizing enzymes in this excretory process. Male and female rats were given i.p. injections of tritiated 3,4-benzpyrene (10 mg/kg), and in some cases rats were pretreated with agents which induce microsomal drug-metabolizing enzymes such as phenobarbital, methylcholanthrene, or 3,4-benzpyrene. Pretreatment with these agents greatly enhanced the rate of biliary excretion of 3,4-benzpyrene. Pretreatment with methylcholanthrene led to the excretion in 1 hr of 32.7% of the compound, compared to 6.0% for controls. Both the rates of metabolism and of biliary excretion were enhanced to a similar extent throughout the induction period. Emetine inhibited both the metabolism and the rate of biliary excretion of 3,4-benzpyrene approximately 50%. Male rats both metabolized 3,4-benzpyrene and subsequently excreted its metabolites in the bile at rates approximately 2.5 times the respective rates in females. When 3,4-benzpyrene metabolites were injected, their biliary excretion rate greatly exceeded the rate seen when 3,4-benzpyrene itself was injected. This greater rate of excretion could not be further increased by treatment with inducing agents. The induction by methylcholanthrene of both the metabolism and the biliary excretion of 3,4-benzpyrene was partially blocked by ethionine.

Apparently, the acceleration of 3,4-benzpyrene excretion by inducing agents was attributable to the enhancement of conversion of the carcinogen to its metabolites; furthermore, conversion to metabolites seemed to be the rate-limiting step in the biliary excretion of 3,4-benzpyrene.

0459 IN VIVO DECREASE IN LIVER BENZPYRENE
HYDROXYLASE ACTIVITY AFTER CARBON MONOXIDE
INHALATION. (Fr.) Rondia, D. (Fac. Med. U. Liege,
Belgium). *C R Acad Sci* 271(6):617-619, 1970.

The effect of carbon monoxide on cytochrome P-450 associated enzyme systems (involved in detoxication mechanisms of the liver) was studied in male Wistar rats. Groups, consisting of 10 experimental and 10 control animals each, were exposed to carbon monoxide, 60 ppm for 120 hr, 100 ppm for 168 hr and 150 ppm for 48 and 120 hrs. All animals were sacrificed at the end of the exposure period, and their liver homogenates with the necessary coenzymes and 0.1 mmole of benzpyrene, were incubated at 37°C for 10 min. Benzpyrene hydroxylase activity was measured by both the determination of the nonmetabolized benzpyrene and the determination of the product, 3-hydroxybenzpyrene. Exposure to 60 ppm carbon monoxide lowered the enzyme activity by 13% and exposure to 20 ppm carbon monoxide lowered the activity by 20%. The enzyme activity appeared to increase during the first 48 hr of exposure with 150 ppm, but decreased by 25% after 120 hr of carbon monoxide inhalation. Slight anoxia seemed to modify the composition of the reticuloendothelial system of rat liver, and carbon monoxide seemed to be acting specifically on one of the liver hydroxylation electron transfer systems, where the involvement of cytochrome P-450 could not be confirmed by spectrophotometry.

0460 INHIBITORY ACTION OF CHEMICAL CARCINOGENS
ON MITOSES OF RAT LUNG CELL CULTURES. I.
3,4-BENZPYRENE. (Fr.) Guerin, M. (Inst. Res. Sci.
Cancer, Villejuif, France), I. Chouroulinkov and P.
Lazar. *C R Soc Biol* 164(2):234-238, 1970.

The antimitotic effects of 3,4-benzpyrene were studied in rat embryo lung cell cultures (Parker 199 media treated with 20% calf serum). 3,4-Benzpyrene added as a 0.1% acetone solution at a ratio of 5γ/ml culture media inhibited mitosis completely. When samples treated with 0, 0.001, 0.01, 0.1 and 1.0γ were maintained for 7 days, the mitotic index decreased correspondingly to give the following values; 7.8, 7.5, 4.4, 0.3 and 0, resp. Mitotic inhibition was attributed to a specific action of 3,4-benzpyrene on the mitotic cycle of the cell rather than to its toxic effects. Similar antimitotic effects induced by other chemical carcinogens are reviewed.

0461 SOLUBILITY OF POLYCYCLIC HYDROCARBONS IN
SERA. (Ger.) Obrikat, H. (Hyg. Inst. Hum-
boldt U., Berlin, Germany) and K. Wettig. *Arch Ge-
schwulstforsch* 35(4):326-337, 1970.

The increase in the number of cases of bronchial carcinoma is attributed to air pollution largely with carcinogenic polycyclic hydrocarbons. The elimination of these particles from the lungs is dependent upon their solubility in the body fluids. This property was investigated in the sera of calf, horse and man with pyrene and 3,4-benzpyrene. It was established that the carcinogenic benzpyrene is less soluble than the noncarcinogenic pyrene, and its solubility in human serum is significantly greater than in calf or horse sera. The blood group or Rh factor did not affect the solubility, and an increase in gamma globulin concentration decreased the solubility. Because an inflammatory process often precedes cancerous events and serum lipids are increased, benzpyrene absorption is facilitated. It is postulated that reduced ciliary action in inflammatory processes of the respiratory tract influences the elimination of particles adversely, and carcinogenesis in such instances is more likely to occur.

- 0462 EFFECT OF METHYLCHOLANTHRENE ON BIOSYNTHESIS AND METABOLISM OF BILE ACIDS. (E.) Johansson, G. (Karolinska Inst., Stockholm, Sweden). *Biochem Pharmacol* 19(10):2817-2820, 1970.

The effect of methylcholanthrene on hydroxylation reactions involved in the biosynthesis and metabolism of bile acids was investigated in male rats. Rats were given daily injections of 25 mg/kg 3-methylcholanthrene for 3 days. Hydroxylation substrates were incubated with liver homogenates from these rats, and thin-layer chromatography of extracts of incubations with the different neutral steroids and 3,4-benzpyrene was performed. The patterns of hydroxylation products were the same in control rats and in methylcholanthrene-treated rats. Total conversion of cholesterol, cholest-5-ene-3 β , 7 α -diol conversion into 7 α -hydroxycholest-4-en-3-one, and hydroxylation of 7 α -hydroxycholest-4-en-3-one were similar in treated and control animals. The rate of 7 α -hydroxylation of taurodeoxycholic acid was not affected by methylcholanthrene treatment. The 6 β -hydroxylation of taurochenodeoxycholic acid and lithocholic acid was less effective in methylcholanthrene-treated rats than in control rats, with hydroxylation rates for taurochenodeoxycholic and lithocholic acids being, resp., 2.2 and 1.8 times faster in control rats than in treated rats. In methylcholanthrene-treated rats, however, the extent of formation of hydroxylated derivatives of 3,4-benzpyrene was 6.8 times greater than in controls. Apparently, methylcholanthrene does not affect any rate-limiting component of the hydroxylations involved in the biosynthesis of bile acids.

- 0463 ENHANCED INITIATION OF RNA CHAINS IN LIVER AFTER ADMINISTRATION OF 3-METHYLCHOLANTHRENE. (E.) Bresnick, E. (Baylor Coll. Med., Houston, Tex.) *Biochem Biophys Acta* 217(1):204-206, 1970.

Chromatin prepared from liver nuclei (method of Dingman and Sporn) of 3-methylcholanthrene-treated

(20 mg/kg, i.p.) rats was incubated with RNA polymerase from *Escherichia coli* in the presence of γ -³²P-ATP to determine the effect of methylcholanthrene (MC) on the initiation of RNA chains. A 10 min the amount of ATP incorporation into RNA 1.6 times greater with MC-chromatin (8000 cpm) with control-chromatin (5000 cpm), and the incorporation required RNA polymerase, chromatin, and divalent cations. Pancreatic ribonuclease (5 μ) added to the incubation mixture at zero time inhibited both the control and experimental reaction by 80%; when the RNA product was treated with a line phosphatase the ³²P label was acid-soluble and norite-non-absorbable while treatment with creatine ribonuclease and hydrolysis left the ³²P label acid-soluble but norite-absorbable, indicating that the label was located in the phosphodiester linkage at the terminus of the RNA chain.

- 0464 INDUCTION OF DRUG METABOLISM: V. INDEPENDENT FORMATION OF CYTOCHROMES P-450 AND P₁-450 IN RATS TREATED WITH PHENOBARBITAL AND 3-METHYLCHOLANTHRENE SIMULTANEOUSLY. (E.) Bidh K. (U. Minnesota Coll. Med. Sci., Minneapolis) G. J. Mannering. *Molec Pharmacol* 6(6):697-701, 1970.

The effects of phenobarbital (40 mg/kg/day, i.p.) and 3-methylcholanthrene (20 mg/kg/day, i.p.) administered alone or in combination on the induction of cytochromes P-450 and P₁-450 were studied in Simonsen rats. 3-Methylcholanthrene caused the formation of cytochrome P₁-450, increased aniline binding, the A₄₅₅:A₄₃₀ ratio, and 3-methyl-4-methylaminoazobenzene N-demethylase activity, increased hexobarbital binding, and did not affect ethylmorphine N-demethylase activity, while phenobarbital caused the formation of cytochrome P-450 and increased all of the above measurements except the A₄₅₅:A₄₃₀ ratio. Simultaneous administration elevated the aniline and hexobarbital binding, the 3-methyl-4-methylaminoazobenzene N-demethylase activity nearly to the sums of each of these measurements when the agents were administered singly. Apparently cytochromes P-450 and P₁-450 are synthesized independently of each other since the simultaneous administration of the 2 agents results in the formation of both cytochromes.

- 0465 OXYGEN CONSUMPTION AND HISTOLOGICAL CHANGES OF MOUSE SKIN DURING THE INDUCTION OF CUTANEOUS SARCOMA WITH METHYLCHOLANTHRENE. (E.) Zador, S. (Inst. Res. Sci. Cancer, Villejuif, France) *Virchow Arch Zellpath* 6(1):72-78, 1970.

The carcinogen 3-methylcholanthrene was injected s.c. in amounts of 1 mg in olive oil in mice, the consumption of oxygen and lactic acid was measured in tissue slices from the injection site during the development of sarcomata. Oxygen consumption tended to increase slightly with time in treated and in untreated animals, an abrupt increase when sarcomas developed was seen (2.14 μ l/hr/mg before appearance of tumor and 2.58 μ l/6 hr/mg after tumor appearance). Lactic acid production

increased approximately 75% as soon as sarcomas developed. No systematic influence on hair growth was found in the carcinogen-treated animals, nor could any other qualitative alterations be demonstrated.

0466 MECHANISM OF 3-METHYLCHOLANTHRENE-INDUCED INHIBITION OF DIMETHYLNITROSAMINE DEMETHYLASE IN RAT LIVER. (E.) Venkatesan, N. (US Publ. Hlth. Service Hosp., New Orleans, La.), M. F. Argus, and J. C. Arcos. *Cancer Res* 30(10):2556-2562, 1970.

Immature male rats were given i.p. injections of 3-methylcholanthrene (30 mg/kg body wt) to investigate the time course of DMN demethylase inhibition. At 10 hr after injection of the inhibitor, DMN activity was reduced by 17.7%, inhibition rising to 37.6% at 15 hr. DMN demethylase activity in liver microsome preparations of treated rats was similar to that in untreated livers, indicating that there is no endogenous DMN demethylase inhibitor in rat livers. Kinetic studies on DMN demethylase activity showed that the enzyme in both 3-methylcholanthrene-pre-treated rats and untreated rats had similar K_m values (control K_m being $22.6 \times 10^{-5}M$, and treated K_m being $22.0 \times 10^{-5}M$). The V_{max} for treated and untreated rats were significantly different, treated and untreated rats showing values of 8.7 μ moles HCHO/mg protein/30 min, and 12.2 μ moles, resp. Phenobarbital treatment also inhibited DMN demethylase, though to a lesser extent than 3-methylcholanthrene. No sex difference was detected in DMN demethylase sensitivity to inhibition by 3-methylcholanthrene in young adult male and female rats. Furthermore, no change in DMN demethylase activity was brought about by prolonged treatment of immature female rats with 15 mg/ml of 17 α -methyltestosterone. The inhibitory effects of actinomycin D (20 μ g) or puromycin (2 mg) administered to rats on DMN demethylase inhibition by 3-methylcholanthrene were additive, suggesting that the hydrocarbon and the antibiotics do not act at the same target. 3-Methylcholanthrene appears to affect the gene which codes for DMN demethylase.

0467 VIRUS-LIKE PARTICLES IN CHEMICALLY INDUCED SARCOMAS IN HIGH- AND LOW-LEUKEMIA STRAINS OF MICE. (E.) Liebelt, R. A. (Baylor Coll. Med., Houston, Tex.), S. Suzuki, A. G. Liebelt and M. Lane. *Cancer Res* 30(9):2438-2448, 1970.

The incidence of sarcomas and virus-like particles was determined in high-leukemia strains of mice (AKR/Ki and C58/Ki) following a single injection of 3,4-benzpyrene (0.004 mg/g, s.c.) and in newborn AKR mice following 3-methylcholanthrene (0.05 ml of 0.5% in olive oil). Sarcomas developed with comparable frequency in the low-leukemia strains (21-50% incidence) after 3,4-benzpyrene, but the incidence was much lower in the high-leukemia strains (3.6% and 8%) after benzpyrene, although in the high-leukemia strain AKR the incidence was relatively high (40%) after 3-methylcholanthrene. Type C murine leukemia virus particles were found abundantly in pri-

mary and transplanted sarcomas and in normal tissue of AKR and C58 strains, less frequently in primary and transplanted sarcomas in BALB/cf, C3H/f, and C3H mice, and not at all in either sarcomas or normal tissue of Af mice. Type A virus particles were seen in sarcomas and normal tissue of AKR and C58 mice but not in any of the other strains. Cell-free extracts of Af tumor tissue caused reticular tissue, lung and liver tumors in BALB/cf, C3Hf and C57BL mice, but none of the animals developed sarcomas. Cell-free extracts of C58 virus were injected into newborn BALB/cf mice and significantly increased the incidence of lung tumors only after material from a sixth generation transplant was used and not after a first generation transplant; cell-free extracts of AKR injected into newborn BALB/cf mice showed no lung tumors or reticular tissue neoplasms in the injected mice compared to a 17-19% incidence of lung tumors and a 7-28% incidence of leukemia in controls. A complicated interaction between host genetic factors and the different viruses is suggested.

0468 SEARCH FOR COMMON ANTIGENICITIES AMONG TWENTY-FIVE SARCOMAS INDUCED BY METHYLCHOLANTHRENE. (E.) Basombrio, M. A. (Inst. Cancer Res., Fox Chase, Philadelphia, Pa.). *Cancer Res* 30(10):2458-2462, 1970.

Female mice were implanted with millipore discs containing 5% of 3-methylcholanthrene, and the ensuing tumors (pleomorphic sarcomas and rhabdomyosarcomas) were excised preparatory to challenging the established tumor immunity with various intradermal inocula of tumor cell suspensions. The aim was to investigate the possibility that antigenic specificities may be shared by 25 tested sarcomas. Two modalities of the transplantation test for antigenicity, designated as "multiple challenge" and "multiple immunization," were used. The first consisted of immunizing mice with 1 tumor and testing in them the rejection of the same and others when threshold cell doses were injected intradermally in different skin sites. Each one of the tumors was clearly rejected in mice immunized with the same tumor line, but it grew regularly in mice immunized with each one of the other tumors and in controls. There appeared to be some instances of cross-immunization in a first screening of the 90 possible tests between 10 tumors, but no such cases could be reproduced for any pair of tumors. Evidently, each of 10 tumors tested had a different antigenic type. Fifteen tumors were studied in multiple immunization experiments consisting of inducing immunity simultaneously with 4 tumors and challenging this immunity with a single, different one. No stable cross-protection was revealed in 13 out of 14 such tests. One tumor pool was selected, however, which cross-immunized against a different tumor in 3 out of 3 tests; this pool failed to protect against 4 other tumors. Totally and partially shared antigenic components among methylcholanthrene induced tumors, as evidenced by rejection of tumor cell inocula, appear to be extremely rare phenomena.

- 0469 COMPARATIVE DISTRIBUTION OF DEHYDROGENASES IN MOUSE EPIDERMOID EPITHELIOMA AND NORMAL SKIN. (Fr.) Dokov, V. K. (Lab. Anat. U. Liege, Belgium), M. A. Gerebtzoff and P. Minet. *C R Soc Biol* 164(3):675-676, 1970.

Dehydrogenase activities in a methylcholanthrene-induced epithelioma (C3H mouse skin) were studied 15 days after transplantation and compared to levels in normal mouse epidermis. The distribution of glutamate dehydrogenase in the cytoplasm of tumor cells was higher at the chromosomal level of mitotic cells (mainly in metaphasic stages) and generally higher than in normal epidermis, due to enhanced amino acid biosynthesis. Activities of succinate, glucose-6-phosphate and isocitrate dehydrogenases were highest in the cytoplasm of glandular structures. Lactate dehydrogenase activities were high in all tumor cells, and no differences between isoenzyme activities were observed. The pseudokeratinization process of epidermoid epithelioma cells was associated with high glucose-6-phosphate and isocitrate dehydrogenase levels, indicating an enhancement of the pentose phosphate shunt, the Krebs cycle and nucleoprotein synthesis. The increased levels of dehydrogenase activity in tumor cells appear to be associated with the proliferative process of the tumor cell population, with higher energy requirements, glucose degradation and protein synthesis rates than normal cells.

- 0470 SKIN TUMORS IN ACI/N RATS INDUCED BY 3-METHYLCHOLANTHRENE AND 4-DIMETHYLAMINOSTILBENE. (E.) Takayama, S. (Cancer Inst. Tokyo, Japan). *Gann* 61(4):367-371, 1970.

The effect of p.o. 4-dimethylaminostilbene on skin tumor induction by topical application of 3-methylcholanthrene was studied in ACI/N rats. Groups of male and female rats were treated in one of 4 ways; painting with 0.3% 3-methylcholanthrene in acetone (20 wk), 3-methylcholanthrene painting and 0.05% 4-dimethylaminostilbene diet (20 wk), 4-dimethylaminostilbene diet alone (20 wk), and acetone painting alone (20 wk). Skin painting with 3-methylcholanthrene produced skin tumors in 19 of 20 rats with an average latent period of 32 wk. Painting with the compound combined with dietary 4-dimethylaminostilbene produced tumors in 17 of 18 rats with an average latent period of 30 wk. Dietary 4-dimethylaminostilbene produced no skin tumors in 17 of 20 rats (the remaining 3 rats having died before the 10th wk) and no tumors were found in 28 acetone-painted rats. The skin tumors produced were usually multiple in occurrence, and trichoepitheliomas were most abundant (50%) in animals painted with 3-methylcholanthrene, while basal cell carcinomas were most common (44%) in the group treated with 3-methylcholanthrene and 4-dimethylaminostilbene.

- 0471 POSSIBLE ASSOCIATION OF EMBRYONAL ANTIGEN(S) WITH SEVERAL PRIMARY 3-METHYLCHOLANTHRENE-INDUCED MURINE SARCOMAS. (E.) Brawn, R. J. (U. Washington Med. Sch., Seattle). *Int J Cancer* 6(2):245-249, 1970.

The effects of lymph-node cells (5×10^6 cells) from multiparous pregnant BALB/c mice and from age-matched BALB/c virgin female mice on *in vitro* colony formation of several lines of primary 3-methylcholanthrene-induced murine sarcomas were compared. Lymphocytes from multiparous pregnant mice significantly inhibited the colony formation of the induced sarcoma compared to lymphocytes from virgin controls, but did not inhibit the growth of normal fibroblast tissue. Lymph-node cells from the pregnant mice mediate an immune response against embryonal sarcoma associated only with cultured MCA-induced neoplastic cells, although the observed response may be non-specific and related to the physiological differences between pregnant and virgin mice.

- 0472 ELECTRONIC STRUCTURES AND MECHANISM OF CARCINOGENICITY FOR ALKYL NITROSAMINES. (E.) Nagata, C. (Nat'l. Cancer Ctr. Res. Inst., Tokyo, Japan) and A. Imamura. *Gann* 61(2):169-176, 1970.

Electronic structures of a carcinogenic (methyl ethylnitrosamine) and a non-carcinogenic (diallyl nitrosamine) nitroso compound were calculated using the CNDO method (complete neglect of differential overlap), and the electronic states of the proposed metabolic pathways were compared. The most stable structure for methylethylnitrosamine was estimated by comparing the calculated total energies for possible stereo-structures; the calculated electrostatic charges for the presumed stable structures of methylethylnitrosamine and for diallylnitrosamine are compatible with the α -carbon hydroxylation subsequent heterolysis. The energy increment (energy of the products minus the total energy of reactants) calculated for each step in the assumed metabolic pathway (enzymic hydroxylation, heterolysis, and alkylation through a bimolecular nucleophilic reaction or through a monomolecular nucleophilic substitution) was lower for the non-carcinogenic agent in all the reactions except in the alkylation preceding an S_N2 mechanism (bimolecular nucleophilic reaction), indicating that this is the critical rate-limiting step in the carcinogenic action of nitrosamine compounds.

- 0473 METABOLISM OF DIMETHYLNITROSAMINE BY HUMAN LIVER SLICES *IN VITRO*. (E.) Montesano, R. (Middlesex Hosp. Med. Sch., London, England) and P. N. Magee. *Nature* 228(5267):174, 1970.

Human liver slices were incubated with ^{14}C -dimethylnitrosamine in order to investigate the metabolism of this compound by liver slices as an indicator of possible carcinogenic effects of the compound in man. The production of labeled carbon dioxide from methylation of slice nucleic acids was used to monitor dimethylnitrosamine metabolism. These results compared to those of similar experiments using rat liver slices showed that the respiration rate of the rat liver slices ($760 \mu l O_2/g$ wet wt/hr) was higher than the respiration rate of the human liver slices ($240 \mu l O_2/g$ wet wt/hr), and that rat slices produced more $^{14}CO_2$ in 100 min (5.2%) than did human slices (3.0%). Nucleic acid me-

ation rates were lower for human slices (0.13%) than for rat slices (0.19%). The results indicate that human liver can metabolize dimethylnitrosamine at a rate comparable with rat liver; the similar levels of nucleic acid methylation in the 2 species suggest that man may be as sensitive as the rat to the carcinogenic effects of this compound.

- 0474 AMINO ACID INDUCTION AND CARBOHYDRATE REPRESSION OF DIMETHYLNITROSAMINE DEMETHYLASE IN RAT LIVER. (E.) Venkatesan, N. (US Publ. Hlth. Service Hosp., New Orleans, La.), J. C. Arcos and M. F. Argus. *Cancer Res* 30(10):2563-2567, 1970.

The effect on dimethylnitrosamine (DMN) demethylase in rat liver of starvation and treatment with various agents including 3-methylcholanthrene was investigated. Male rats were starved or fed, and administered 3-methylcholanthrene (40 mg/kg), actinomycin D (20 µg), casein, glucose, or cellulose. Starvation more than doubled the demethylase activity measured in (nmole HCHO/mg protein/40 min) from 17 in fed to 37 in starved rats, resp. Treatment with 3-methylcholanthrene inhibited the enzyme to the same extent in starved animals as it did in fed animals, DMN methylase activity measuring 9 and 24 nmole HCHO/mg protein/40 min, resp., for methylcholanthrene-fed and methylcholanthrene-starved animals. Starvation did not cause significant increases in the K_m of the enzyme; however, the V_{max} was significantly elevated in starved animals (51.7% increase), indicating an increase in demethylase. The starvation-induced DMN demethylase activity was blocked when actinomycin D was administered to rats throughout the fasting period. The findings with actinomycin D indicate that the starvation-induced increase of demethylase activity was due to original protein synthesis, a hypothesis which is consistent with the observed increase in V_{max} of the enzyme. Ingestion of glucose markedly inhibited demethylase activity compared to the starved state; rats fed glucose had DMN demethylase activity of 17.4 nmole HCHO/mg protein/40 min, and starved animals had an activity of 44.6 nmole HCHO/mg protein/40 min. Casein stimulated demethylase activity to 59.7, and cellulose had no effect on the activity.

- 0475 INVESTIGATION OF RIBOSOMAL PROTEINS: III. ALTERATIONS OF THE RIBOSOMAL FERRITIN-FRACTION INDUCED BY HEPATOTROPIC CARCINOGENS. (Ger.) Meyer-Bertenrath, J. G. (St. Hosp. Hanau, Germany) and W. Domschke. *Z Naturforsch* 25(7):744-748, 1970.

To determine the effect on liver ribosomes of carcinogenic agents such as N-nitrosomorpholine (NNM), diethylnitrosamine (DENA) or thioacetamide (TAA), an investigation was carried out in rats pretreated for 60 days with a 12 mg/100 ml concentration of NNM or DENA and a 30 mg/100 ml TAA solution for 6 weeks. Determinations of the Michaelis constants of ribonuclease, with ribosome or ferritin-free subribosomal particles demonstrated that the ribosomes from the carcinogen-pretreated animals contained RNA structures with a different ferritin fraction than did the normal ribosomes, the Michaelis con-

stant being 100-fold higher for the former. The ribosomal ferritin fraction remained unchanged for at least 2 months following the removal of the carcinogenic agent. It is suggested that this test can be applied to human liver biopsies.

- 0476 TOXICITY AND ONCOGENICITY OF NITROSOMETHYLANILINE AND NITROSOMETHYLCYCLOHEXYLAMINE.

(E.) Goodall, C. M. (Natl. Cancer Res. Lab., U. Otago, New Zealand), W. Lijinsky, L. Tomatis and C. E. M. Wenyon. *Toxic Appl Pharmacol* 17(2):426-432, 1970.

From acute and chronic toxicity studies of N-nitroso-N-methylaniline (NMA) and N-nitroso-N-methylcyclohexylamine (NMC) in rats, mice and hamsters, 3-day LD₅₀ values were determined. The LD₅₀ (mg/kg) of NMA (by gavage) was 336 in male rats, 225 in female rats, and 150 in hamsters; the LD₅₀ of NMC (by gavage) was 80 in male rats, 180 in female rats, 168 in hamsters, and 57 in mice (the convulsant effect of NMC was prevented by anesthesia), and the LD₅₀ for injections of NMC (saturated solution in water, i.p.) in male rats was 28 mg/kg. Neither compound produced apparent histologic lesions of liver or other organs. Chronic studies of NMA and NMC administered by gavage (7.5 mg, 2 days/wk and 2 mg, 2 days/wk, resp.) and in drinking water (1.0, 2.0, and 4.0 mg, 5 days/wk for each compound) indicated that both NMA and NMC are potent carcinogens producing sessile papillomas and squamous carcinomas in the upper gastrointestinal tract and that both produced liver damage after prolonged treatment.

- 0477 THE TRANSPLACENTAL EFFECT OF DIMETHYLNITROSAMINE IN ORGAN CULTURES OF THE KIDNEYS. (Rus.) Sorokina, Yu. D. (Inst. Clin. and Exp. Oncol., Moscow, USSR) *Biull Eksp Biol Med* 70(8):77-81, 1970.

Dimethylnitrosamine administered to C3HA pregnant mice (0.25 mg/kg, s.c., 2 days before explantation) led to considerable changes in embryo kidney organ cultures which had been explanted at 19-21 days of pregnancy. Diffuse hyperplasia of the tubular epithelium manifested by partial or total epithelization of the explants was noticed 2 wk after explantation. After 10 days of culture maintenance papillary outgrowths (hyperplastic epithelial foci) appeared. Furthermore, the transplacental effect of the carcinogen determined a better survival of the embryo explants at the later stages of the investigation. The diffuse and focal epithelial hyperplasia possibly constitute the first stages of pretumoral transformation.

- 0478 TRANSPLACENTAL INDUCTION OF MALIGNANT TUMORS BY ORAL ADMINISTRATION OF ETHYLUREA AND NITRITE TO RATS. (Ger.) Evankovic, S. (German Cancer Res. Ctr. Heidelberg, Germany) and R. Preussman. *Naturwissenschaften* 57(9):460, 1970.

The endogenous synthesis of nitrosoamides demonstrable in transplacental carcinogenesis was illustrated in an experiment on 7 pregnant rats, by the administration of ethylurea at 100 mg/kg 13-23 days after coitus and 50 mg/kg of sodium nitrite

CHEMICAL CARCINOGENESIS

directly afterwards by stomach tube. Of the newborn animals 13/19 survived, and 10 rats died between 77-211 days. These latter showed neurogenic tumors and a leukemia, resp. The administration of either ethylurea or sodium nitrite alone did not demonstrate any tumor formation. The tumors described are typical of the transplacental action of ethylnitrosourea and demonstrate their origin in the gastrointestinal tract.

- 0479 TUMORS OF OROPHARYNX AND FACE IN NZO, NZB, AND NZY MICE TREATED WITH N-NITROSO ALI-CYCLIC IMINES. (E.) Geary, C. P. (Natl. Cancer Res. Lab., U. Otago, New Zealand), C. M. Goodall, M. Bielschowsky and W. Lijinsky. *Pathology* 2(4):261-268, 1970.

The incidence and pathology of oropharyngeal and facial tumors in NZB, NZO, and NZY/B1 mice following the administration of N-nitrosohexamethyleneimine (NHM) or N-nitrosopentamethyleneimine (NPIP) in drinking water (200 mg/l) over two 4-week periods were studied. Fourteen of the 135 mice given NHM and 3 of the 22 given NPIP developed the tumors, indicating that the oncogenic capacity of both ali-cyclic nitroso imines were similar. No significant difference in tumor incidence was noted between male and female mice (10 and 7, resp.), but a genetic influence was suggested by the 12.5% incidence in the closely related NZB and NZO/B1 strains compared to the 3.2% incidence in the unrelated NZY/B1 strain. All the tumors were squamous epithelial neoplasms (except for 1 histiocytic malignant lymphoma) and were invasive carcinomata (frequently infiltrating adjacent connective tissue and muscle fascial planes) showing varying degrees of differentiation.

- 0480 CYTOPHOTOMETRY OF THE TRACHEAL MUCOSA AND OF THE DENA-INDUCED PAPILLOMATA OF THE SYRIAN GOLDEN HAMSTER: QUANTITATIVE STUDIES OF DE-DIFFERENTIATION. (Ger.) Tasca, C. (German Cancer Res. Ctr., Heidelberg), D. Haag and K. Goerttler. *Z Krebsforsch* 74(4):355-367, 1970.

Cytophotometric criteria (based on 3700 nuclei) of differences between normal and neoplastic cells are described. The tissues used in the comparative study were taken from pregnant golden hamsters in whom tracheal papillomata were induced by means of DENA (50 mg/kg diethylnitrosoamine, s.c.) 8 days following insemination. The mothers and progeny were sacrificed 6 months following the treatment and the trachea was prepared for cytological examination. With UV absorption, the unstained histological preparations of normal tracheal mucosa revealed an intense darkening of the cell nuclei due to the absorption of nucleic acid; although the nuclei of the papillomata had almost the same DNA content as normal tissue, they were about twice as large and showed only slight UV absorption. This difference was also observed in the variously stained cells. An analysis of the papillomata nuclei revealed a diminished correlation between nuclear volume and content of nucleic acids or histones.

Changes in the nuclear volume, widening in the distribution curve of the histograms, and the decrease in the correlation of nuclear volume and nucleic content were associated with the extent of the malignancy.

- 0481 INDUCTION OF BLADDER TUMORS IN MICE WITH DIBUTYLNITROSAMINE. (E.) Bertram, J. S. (Christie Hosp., Manchester, England) and A. W. *Brit J Cancer* 24(2):352-359, 1970.

The carcinogenic activity of high doses (30 mg/kg/day) and low doses (7.6 mg/kg/day) of dibutylamine (DBN) given continuously in drinking water was studied in C57BL/6 mice. The high dose produced bladder tumors in 44 mice (48%) after a cumulative dose of 7400 mg/kg with a tumor induction time of 240 days, while the low dose produced bladder tumors in 19 mice (21%) after a mean cumulative dose of 2000 mg/kg with an induction time of 260 days. Bladder tumors occurred predominantly in males with the male to female ratios of 4.4 and 8.5 at the high and low doses, resp. Esophageal tumors were observed in all but 9 animals, while 5 animals receiving the lower dose of DBN developed forestomach carcinomas, and 13 animals (5 in the higher dose group and 8 in the lower dose group) developed tumors of the soft palate or tongue.

- 0482 UPPER RESPIRATORY TRACT TUMORS INDUCED IN SYRIAN HAMSTERS BY N-METHYL-N-NITROSOUREA. (E.) Herrold, K. McD. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *Int J Cancer* 6(2):217-222, 1970.

The upper respiratory tract of Syrian hamsters was histologically examined following intratracheal instillation of N-nitroso-N-methylurea (0.5 mg/kg daily for 2½ months). Respiratory distress occurred in 8 animals after 5 to 7 months, 1 animal died at 8 months, and 1 animal survived to 11 months. Tumors developed in the nasopharyngeal tube, pharynx, trachea, bronchi, esophagus, and forestomach wall. Of the 10 hamsters exhibiting multiple tumors, although no distant metastases were observed. All tumors were epidermoid carcinomas and many were centric in origin. N-nitroso-N-methylurea is a highly effective carcinogen affecting the upper respiratory tract of Syrian hamsters.

- 0483 SELECTIVE INDUCTION OF CARCINOMAS OF THE GLANDULAR STOMACH BY N-METHYL-N-NITROSO-N'-ACETYLUREA IN RATS. (Ger.) Druckrey, H. (Max Planck Inst. Immunobiol., Freiburg, Germany), Ivankovic and R. Preussmann. *Z Krebsforsch* 75:23-33, 1970.

A model for the induction of gastric cancer is presented; N-methyl-N-nitroso-N'-acetylurea administered to 13 BD rats (2mg/kg in drinking water 5 times for 330 days) produced carcinoma of the glandular stomach in the pyloric region in all of the animals approximately 80 days after the end of the treatment. Another group of 11 rats were given 4 mg/kg under the same conditions as above. C

surviving rats, 8 had extended and partially perforated gastric adenocarcinoma morphologically similar to the ones developed in the lower dose group, except for 2 cases of polymorphic sarcomas. Two rats of the higher dose group also had cerebral glioma, and 2 rats had malignant neurinoma of the peripheral nervous system, indicating absorptive effects at the nervous system level. A considerable similarity with human gastric adenoma was observed.

- 0484 EFFECT OF N-METHYL-N'-NITRO-N-NITROSOGUANIDINE ON THE CELL CYCLE AND CHROMOSOMES OF HUMAN EMBRYONIC LUNG CELL. (E.) Kelly, F. (Div. Pharmacol. Toxic., Food Drug Admin., Washington, D. C.) and M. Legator. *Mutat Res* 10(3):237-246, 1970.

The effects of N-methyl-N'-nitro-N-nitrosoguanidine (MNNG, 0.5 µg and 1.0 µg/ml) on DNA synthesis, cell cycle, and chromosome structure of random and synchronized populations of heteroploid human embryonic lung cells (L-132) were determined by autoradiography and liquid scintillation techniques. The mitotic index of cells exposed to MNNG decreased to less than 10% of control values after 16 hr, then slowly increased toward normal levels. Cells exposed to MNNG while in the S phase remained in S phase while cells in the G₁ stage proceeded into S phase where the rate of DNA synthesis dropped 43% (1600 cpm to 900 cpm), although ³H-thymidine incorporation was increased (60% compared to 35% in control cells). Cells in the G₂ phase were not affected. MNNG lengthened the S phase (7 hr to 17 hr) and the time required for cells in the G₁ phase to reach division (9 hr to 16 hr). Chromosomes of cells in G₁ and early and mid-S stages were sensitive to the MNNG and exhibited chromatid breaks and exchange configurations, although late S and G₂ phase cells showed no chromosome abnormalities at metaphase of the first division after exposure.

- 0485 SPECIFIC EXCISION OF METHYLATION PRODUCTS FROM DNA OF *ESCHERICHIA COLI* TREATED WITH N-METHYL-N'-NITRO-N-NITROSOGUANIDINE. (E.) Lawley, P. D. (Roy. Cancer Hosp., London, England) and D. J. Orr. *Chem Biol Interact* 2(2):154-157, 1970.

Specific enzymatic removal (excision) of products of monofunctional alkylation from the DNA of *E. coli* by the mutagen and carcinogen N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) was investigated. *E. coli* cultures were incubated with doses of tritium labeled MNNG in amounts of 100 and 1000 µg/ml, the DNA isolated, and the excision products determined. The major methylated component in DNA was 7-methylguanine (78%) at MNNG concentration of 0.74 mM; minor products included 3-methyladenine (2%) and 2-amino-6-methoxypurine (11%). No significant difference was observed between the B/r and B_{s-1} strains of *E. coli*.

- 0486 HISTOLOGY AND HISTOCHEMISTRY OF N-NITROSO-N-METHYLURETHAN INDUCED LESIONS OF THE LUNG IN MICE: WITH SPECIAL REFERENCE TO HYDROLASES. (Fr.) Caulet, T. (Fac. Med. Reims, France) and M. Pluot. *Z Krebsforsch* 74(3):227-235, 1970.

The effect of N-nitroso-N-methylurethan on lung parenchyma was studied in 50 white male mice (Swiss strain, 2 months old). The carcinogen was administered s.c. once a wk for 21 wk (1 mg for the first 5 injections and 0.2 mg thereafter; the mice were sacrificed 15 days-2 months after the end of the treatment. Histological examination revealed areas of eosin-staining cell proliferation, often covering the alveolar pattern; outside these areas the lung parenchyma was severely damaged by a process of reticular hypertrophic pneumonia. The tumor cells had high levels of succinic dehydrogenase, ubiquinone and α-naphthylesterase activities, mainly at the peripheral regions of the proliferative areas; leucine aminopeptidase, alanine aminopeptidase and lipase levels were also high, while cytochrome oxidase, monoamine oxidase, glutamate dehydrogenase and glucose-6-phosphate dehydrogenase activities were low. Acid phosphatase activity was highest in the alveolar macrophages (type III cells) while none or little was found in type I, type II cells and in the tumor cells. ATP-ase levels were high throughout the various lung structures and the tumor foci. Alkaline phosphatase activity was moderate in the bronchial coating, very high in bronchial capillaries and high in the granular alveolar (type II) cells. Minimal alkaline phosphatase activity was found within the tumor cells while very high activities were found in areas of hypertrophic reticular pneumonia and at the capillaries peripheral to the tumor cells, suggesting a possible relationship between alkaline phosphatase activity and the onset of transformation.

- 0487 CARCINOGENIC ACTION OF 8-HYDROXYQUINOLINE. (Rus.) Pliss, G. B. (USSR Minist. Publ. Hlth., Leningrad) and N. I. Volfson. *Vop Onkol* 16(8):67-71, 1970.

Carcinogenicity of 8-hydroxyquinoline (8-OQ) in rats and CC57W mice was studied under the following experimental conditions: I) 70 rats were given 100 mg 8-OQ in sunflower oil suspension s.c. once a wk for 730 days, a total dose of 10,500 mg; II) 39 rats received 15 mg 8-OQ in diet 6 times a wk for 729 days, a total dose of 9,360 mg; III) 62 rats were treated intravaginally with a 20% dist. water suspension of 8-OQ (20 mg twice a wk for 729 days, a total dose of 3,860 mg); IV) 32 mice received 1.5 mg 8-OQ s.c. 3 times monthly for 660 days, a total dose of 97.5 mg; V) 49 mice were given 1.5 mg 8-OQ in the diet 6 times a wk for 660 days, a total of 852 mg; VI) 46 mice were subjected to intercostal skin applications with a 0.75% benzene soln of 8-OQ (1.2 mg 3 times a wk for 656 days, a total dose of 334.8 mg; and VII) 46 mice were subjected to intravaginal applications of 2 mg 8-OQ twice a wk for 812 days, a total dose of 428 mg. The highest incidence of induced tumors occurred in the orally-treated rats

(approximately 50% of the surviving animals) and in the s.c.-treated mice (approximately 40% of the surviving animals) after a latency period of more than 1 yr. Of the rats subjected to s.c. treatment 2 developed lymphosarcoma in the ileocecal region and 2 had fibrosarcomas of the subcutaneous tissue; among the orally-treated rats 1 adenocarcinoma, 2 liver sarcomas, 1 uterine adenocarcinoma, 1 intestinal reticulosarcoma and 5 fibroadenomas of the mammary gland developed; of the intravaginally-treated rats 1 developed uterine cancer associated with a mammary gland fibroadenoma, 1 had a mammary gland fibroadenoma, 2 developed lymphadenosis and 1 developed thyroid cancer. Of the mice subjected to s.c., p.o. and skin application treatment, 7 developed pulmonary adenomas, 2 developed ovarian folliculomas and 5 developed liver hemangiomas. Intravaginal applications of 8-OQ produced no local tumors but 5 mice developed ovarian folliculomas, 4 had lung adenomas and 1 had liver hemangioma. 8-OQ seemed to be a weak carcinogen with resorptive action possibly affecting the hormonal balance.

- 0488 DEVELOPMENT OF INJECTION-SITE SARCOMATA IN RATS: A STUDY OF THE EARLY REACTIVE CHANGES EVOKED BY A CARCINOGENIC NITROQUINOLINE COMPOUND. (E.) Carter, R. L. (Roy. Cancer Hosp., London, England), M. S. C. Birbeck and J. D. B. Roberts. *Brit J Cancer* 24(2):300-311, 1970.

Early reactive changes in the development of sarcoma at the injection site after single doses of polymerized N-nitroso-2,2,4-trimethyl-1,2-dihydroquinoline (NTDQ) were followed in adult (25 mg, s.c.) and newborn (2.5 mg, s.c.) rats using microscopy, autoradiography, and colloidal carbon. The development of lesions proceeded from the non-specific acute inflammatory response of the first 3 days after injection, to more discrete developing granulomata with large mononuclear phagocytes (fibroblasts and macrophages), granulation tissue, and multinucleate giant cells (produced by the fusion of adjacent histiocytes), and finally to the fully developed granulomata at about 10 days. In autoradiographic studies using ^3H -thymidine, the mononuclear cells showed an extensive nuclear labeling during the first 10 days after NTDQ injection which dropped slightly but remained at raised levels throughout the experiment, and the multinucleate giant cells showed no detectable nuclear labeling. Carbon uptake measurements confirmed the lack of proliferative activity in the giant cells and showed minimal phagocytic activity. Colloidal carbon studies also indicated that during the first 5 days after NTDQ injection lymphatic vessels were dilated but local connective tissue barriers quickly closed off the lesions from surrounding dermal tissues.

- 0489 EFFECT OF A POTENT CARCINOGEN, 4-NITROQUINOLINE 1-OXIDE, AND ITS REDUCED FORM, 4-HYDROXYLAMINOQUINOLINE 1-OXIDE, ON BACTERIAL AND BACTERIOPHAGE GENOMES. (E.) Yamamoto, N. (Temple U. Sch. Med., Philadelphia, Pa.), S. Fukuda and H. Takebe. *Cancer Res* 30(10):2532-2537, 1970.

The effect of the carcinogen 4-nitroquinoline-1-oxide (4NQO) and a metabolite of this agent, 4-hydroxylaminoquinoline-1-oxide, on *Salmonella typhimurium* and on bacteriophage activity was investigated. Tumor strains of *S. typhimurium* which could not grow in the presence of 4NQO (4NQO-sensitive mutants) were also sensitive to UV (2 ergs/mm²/sec) and to β -propiolactone. 4NQO-sensitive mutants were of 2 types: host cell reactivation minus mutants which lacked repair activity for the UV-damaged superinfecting phage, and recombination-deficient mutants. Exposure of host cell reactivation minus mutants and wild-type strains to 4NQO, β -propiolactone and UV induced prophages from these strains, but not from recombination-deficient cells; prophage induction from host cell reactivation minus cells was more efficient than prophage induction from wild-type strains. The highly carcinogenic metabolic intermediate of 4NQO, 4-hydroxylaminoquinoline-1-oxide inactivated *Salmonella* phage *in vitro*, while 4NQO itself did not. No difference in inactivation was found on the various indicator hosts when 4-hydroxylaminoquinoline-1-oxide-treated phage was assayed on host cell reactivation minus mutants, on recombination deficient mutants, or on wild-type strains lysogenic for phage P221b. This finding appears to imply that the 4-hydroxylaminoquinoline-1-oxide-damaged phage genome is not reparable by the hosts. No significant increase in recombination was found in recombination-deficient mutants, although the frequency of recombination was increased between the 4-hydroxylaminoquinoline-1-oxide-treated phage and the prophage P221b in wild-type strain cells and host cell reactivation minus mutants. The recombination process between the damaged phage and the prophage P221b seems to be closely related to the bacterial recombination mechanism.

- 0490 EARLY EVENTS IN *IN VITRO* CARCINOGENESIS WITH 4-NITROQUINOLINE-1-OXIDE: II. MECHANISM OF INCORPORATION AND BINDING OF THE CARCINOGEN. Kuroki, T. (Cancer Res. Lab., Tohoku U., Sendai, Japan), R. Kanamaru and H. Sato. *Gann* 61(4):373-382, 1970.

Cultures of hamster embryo cells were treated with a solution of ^{14}C -labeled 4-nitroquinoline-1-oxide (final concentration, $10^{-5.5}\text{M}$) to investigate the mode of incorporation and the binding of this compound to the cells. The carcinogen was incorporated within 30-60 min and was bound to macromolecules of hamster embryo cells with a characteristic time course. The binding persisted over 72 hr after treatment. The rate of incorporation was directly proportional to concentration of the carcinogen and inversely proportional to the cell number. Specific inhibitors of RNA, DNA and protein synthesis such as hydroxyurea, actinomycin D and puromycin had no effect on the incorporation of 4-nitroquinoline-1-oxide. No competent cellular condition or phase in which binding and incorporation of the carcinogen occur appears to exist.

- 0491 NUCLEOLAR ALTERATIONS OF ALVEOLAR EPITHELIAL CELLS IN RATS FOLLOWING A SINGLE INJECTION OF 4-NITROQUINOLINE-1-OXIDE. (E.) Haya

Y. (Shionogi Res. Lab., Osaka, Japan) and T. Hasegawa. *Gann* 61(4):347-352, 1970.

Male rats received a s.c. injection of 4-nitroquinoline-1-oxide suspended in olive oil (15 mg/kg); they were killed 2-48 hr later, and their lungs were subjected to electron microscopic examination to investigate nucleolar alterations in the alveolar epithelial cells. Nucleolar alterations characterized by disintegration of the reticular structure, and segregation of the granular and fibrillar components into separate zones, occurred in the alveolar epithelial cells, both of Type I and II, as well as in the epithelial cells lining the alveolar ducts and the terminal bronchioles. These alterations appeared prominently 6-12 hr after injection. At the 48th hr the reticular structure of the nucleolus appeared to be reorganized in association with an abundance of the granular component. A series of quinoline derivatives with carcinogenic activity, including 4-hydroxyaminoquinoline-1-oxide, 2-methyl-4-nitroquinoline-1-oxide, 6-methyl-4-nitroquinoline-1-oxide and 6-chloro-4-nitroquinoline-1-oxide, was found to produce these nucleolar alterations. Non-carcinogenic quinolines showed no such effect.

0492 COMPARATIVE STUDIES ON THE KINETICS OF THE NEOPLASTIC COMPETENCE IN MICE. (E.) Vesselinovitch, S. D. (Pritzker Sch. Med., U. Chicago, Ill.), N. Mihailovich and L. Itze. *Cancer Res* 30(10):2548-2551, 1970.

Mice of both sexes were administered i.p. injections of urethan (3-12 injections at 3-day intervals commencing on the 1st, 4th or 175th day of life) totaling 1.5-12 mg/g body wt, in order to compare tumor spectra and incidence resulting from the administration of urethan at different age periods. The non-treated controls developed leukemias, hepatomas, lung adenomas, Harderian gland adenomas, and ovarian tumors during their 3rd yr of life. Neonatal exposure to urethan had a positive effect on the development of the same tumor types; the incidence of hepatoma, lung adenoma and Harderian gland adenoma in mice receiving urethan at day one was 86.0%, 30.0% and 8.0%, resp., after a 1-yr observation period. Urethan administered to adult mice at the 6-12 mg/g body wt level resulted in a 2-3 fold increase over controls of lung and Harderian gland adenomas and ovarian tumors which occurred in the 2nd yr of life. The incidence of each of these primary tumors was directly related to the dose of the carcinogen administered. No leukemia developed in the adult animals in spite of the increased dose, while hepatomas were observed in a low incidence only in a group of mice exposed to the highest dose of urethan. Regardless of the tendency of tissues to develop spontaneous tumors, the tumor response to carcinogen with regard to incidence and location appeared to depend on the age of the animal at first exposure to urethan.

0493 PULMONARY ADENOMA IN SWISS MICE RECEIVING URETHANE. VIII. EFFECT OF PHENOBARBITAL. (Fr.) Adenis, L. (Inst. Res. Cancer Lille, France),

M. N. Vlaeminck and J. Driessens. *C R Soc Biol* 64(3):560-562, 1970.

The mechanism of urethan carcinogenesis in mouse lung was studied by using phenobarbital as a structurally related compound. Four groups of animals (25 males and 25 females each, 3-5 months-of-age) were treated as follows: group I received both phenobarbital (0.1 ml of a 2% soln s.c. for 6 consecutive days) and urethan (1 ml of a 4% soln s.c., single dose on the 8th day of the experiment); group II received phenobarbital only (as above); group III received urethan only (as above) and group IV received 1 ml urethan and 15 days later 0.1 ml phenobarbital for 8 consecutive days. The animals were sacrificed at 8 months-of-age. All the animals of group III developed tumors. Animals in group I developed an average of 9 tumors as compared to the average of 1 in group II and 21 in group III, while those in group IV developed an average of 15 tumors. Phenobarbital exhibited no carcinogenic effect, but it had an anti-urethan effect when administered prior to urethan and no effect when injected 15 days after urethan administration.

0494 MEDIASTINAL LYMPHOMA OF THE URETHAN TREATED SWISS MOUSE. X. MICROSCOPY OF GERM-FREE ANIMALS AFTER 10 WEEKS OF TREATMENT. (Fr.) Sacquet, E. (Inst. Res. Cancer Lille, France), F. Puvion, L. Adenis and A. Demaille. *C R Soc Biol* 164(3):557-560, 1970.

The effects of urethan on 35 germ-free Swiss Webster mice 2 months-old were studied. The animals received ethyl urethan (0.1% in drinking water for 10 wk) and were sacrificed 5-9 months from the start of the experiment. Liver, spleen, thymus, lung, kidney and lymphatic ganglia were subjected to routine histological examination and electron microscopy. Both light and electron microscopy revealed morphologically identical lung adenomas in germ-free and conventional animals. Pulmonary epitheliomas occurred in 22 animals while thymic lymphoma with no leukemia as revealed by histology or hematology occurred in 2 germ-free mice. A lower incidence of hyperplasia of splenic Malpighian corpuscles and hepatic angiomatosis was noticed in 22 germ-free animals compared to conventional mice. Ultrastructurally, lymphoid hyperplasia of enlarged cells with large nuclei and free ribosome-rich cytoplasm was observed. Mediastinal lymphomas were rare, compared to the conventional Swiss mouse. No virus particles were detected in the lung tumors or in mediastinal lymphomas in the germ-free mouse.

0495 ISOLATION AND PURIFICATION OF TYPE A VIRUS-LIKE PARTICLES FROM THE CYTOPLASM OF AN ETHYL URETHAN-INDUCED MEDIASTINAL LYMPHOMA. (Fr.) Kerckaert, J. P. (Inst. Res. Cancer, Lille, France), J. Montreuil, M. C. Doyennette, F. Puvion, M. N. Vlaeminck, A. Vebert, A. Demaille and J. Driessens. *C R Acad Sci* 271(6):624-627, 1970.

Highly purified type A2 virus-like particles were obtained from the cytoplasm of urethan-induced

mediastinal lymphoma cells in Swiss mice. Sedimentation of the virus-like particle fraction occurred with the mitochondrial fraction from a 0.25 M sucrose solution homogenate. Addition of Triton X100 to the mitochondrial fraction and isopicnic ultracentrifugation in a continuous cesium chloride gradient resulted in a low yield isolation of the virus-like particle fraction, density = 1.28. This yield was improved by ultracentrifugation of the mitochondrial fraction through a 2-layer system of cesium chloride soln ($d=1.35$ and $d=1.27$), so that clusters of virus-like particles were concentrated at the separation boundary between the 2 cesium chloride soln. Electron microscopy revealed no cytoplasmic contamination of the virus-like particle clusters. Negative dye treatment revealed the presence of bridges of yet unknown nature linking the particles into clusters. Electron microscopy revealed that isolated viral particles were morphologically identical to those contained in the cytoplasm.

- 0496 THE SIGNIFICANCE OF PERINATAL AGE PERIODS AND THE DOSE OF URETHAN ON THE TUMOR PROFILE IN THE MRC RAT. (E.) Kommineni, V. R. C. (U. Nebraska Coll. Med., Omaha), M. Greenblatt, N. Mihailovich and S. D. Vesselinovitch. *Cancer Res* 30(10):2552-2555, 1970.

Fetal, newborn, weanling and young adult rats received i.p. injections of urethan (0.5-6 mg/g body wt) 2 or 4 days prenatally, or at 3-day intervals commencing at 1, 28, or 46 days after birth; the aim was to examine the role of the prenatal, neonatal and postweaning age periods in carcinogenesis at various sites of the body. Rats treated with urethan as newborns showed the highest incidence and the broadest spectrum of neoplasms. At 6 mg/g body wt of urethan, a 30% mortality rate was observed in newborn rats; however, tumor response was clearly more dependent upon the age of the animals at the time of the carcinogenic treatment than upon the administered dose of the carcinogen. Newborn rats developed tumors at specific sites in significantly higher incidence than the animals treated at other age periods. Rats which were exposed to urethan *in utero* developed liver tumors and Anitschkow cell sarcomas of the heart. Neonatally treated animals had gliomas of the brain, neurilemmomas, and embryonal kidney tumors in addition to liver tumors and heart sarcomas. The urethan-treated weanlings showed no heart or brain neoplasms but did develop the other types of tumors with low frequency.

- 0497 THE INDUCTION OF MALIGNANT MELANOMAS IN SYRIAN WHITE HAMSTER BY NEONATAL EXPOSURE TO URETHAN. (E.) Vesselinovitch, S. D. (Pritzker Sch. Med., U. Chicago, Ill.), N. Mihailovitch and W. R. Richter. *Cancer Res* 30(10):2543-2547, 1970.

Hamsters received i.p. injections of urethan (0.5 mg/g body wt) before reaching 24 hr-of-age and on 4 subsequent occasions at 3-day intervals, with the purpose of investigating the induction of malignant melanoma by neonatal exposure to the carcinogen.

The urethan-treated animals developed malignant melanomas which metastasized to regional lymph nodes, lungs, kidneys, and liver (62% of the male and 40% of the females developed tumors). None of the untreated controls showed any melanomas either clinically or at autopsy. The melanoma-bearing hamsters had significantly shorter life-spans than did the untreated controls. (e.g., age at death was 82 wk and 91 wk for treated and untreated hamster resp.) Other tumors developed at a low frequency by the urethan-treated hamster but not by untreated controls included stomach papillomas, hepatocarcinomas, and kidney adenomas.

- 0498 ADRENAL TUMORS AND ENDOCRINE LESIONS INDUCED IN SYRIAN HAMSTERS BY URETHANE INJECTED DURING SUCKLING PERIOD. (E.) Matsuyama, M. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan) and H. Suzuki. *Brit J Cancer* 24(2):312-318, 1970.

Urethan, in 10% saline solution, was injected s.c. into suckling hamsters (1 mg/kg body wt) once a week for 6 wk, with the result that most of the hamsters surviving for more than a year developed nodular hyperplasia of the adrenal cortex and of the pancreatic islets. The experiment was terminated at the end of 124 wk when the last animal died. Eight adrenal cortical tumors, including 2 metastasizing ones, and a β -cell tumor of the pancreatic islets were also found in the 28 treated hamsters. Other lesions included adenomatous hyperplasia of the thyroid, splenic nodules, melanomas of the skin and eyes, papillomas in the forestomach, hemangiomas and cysts in the liver, and an adenocarcinoma of the exocrine pancreas. It may be that there are progressive steps from the hyperplastic nodules to the development of the tumors, a hypothesis supported by the histology of the adrenal lesions.

- 0499 SHORT TERM TEST FOR EVALUATING POTENTIAL CARCINOGENIC ACTIVITY OF TOBACCO CONDENSATES. (E.) Healey, P. (Huntingdon Res. Ctr., London), L. E. Mawdesley-Thomas and D. H. Barry. *Nature* 228(5275):1006, 1970.

Image-analysis techniques were used to estimate specific esterase enzyme activity in the skin of mice painted with tobacco condensates or other known carcinogenic hydrocarbons. Sections were taken of areas of mouse skin painted with various condensates or agents and subjected to image analysis. A direct relationship was found between area of esterase activity and known carcinogenic activity of the compound. High tumor yields (77 and 48% of treated animals) were found for tobacco condensate A in doses of 100 and 60 mg, and this condensate at these doses produced areas of esterase activity of 36 and 64 μm^2 , resp. High esterase activity areas were also found for tobacco condensate C at doses of 36 and 60 mg (areas were 522 and 339 μm^2 , resp). Urethane produced an esterase activity area of 1,392 μm^2 . The area of esterase activity test serves to provide a rapid screen for potential carcinogenic hazards in tobacco condensates.

- 0500 CANCER IN MZ AND DZ TWINS. (E.) Cederlöf, R. (Karolinska Inst., Stockholm, Sweden), B. Floderus and L. Friberg. *Acta Genet Med Gemellol* 19(1-2):69-74, 1970.

The classical twin method was used to analyze mortality and morbidity in cancer and concordance rates for monozygous (MZ) and dizygous (DZ) twins. The influence of smoking habits on cancer development were also analyzed. (Cancer data obtained from the Swedish Cancer Registry and the Registry of Causes of Death). No heredity influence could be shown in the development of cancer although genetic factors may be relevant to the localization of the tumor (1 MZ pair were concordant for cancer of the stomach, 2 MZ pairs were concordant for cancer of the uterus, 1 DZ pair were concordant for cancer of the stomach and 2 DZ pairs were concordant for cancer of the uterus/prostate). A significant difference in cancer morbidity between smokers and nonsmokers was observed only in the male group (63-82 yr of age) where 7.6% of the smokers exhibited cancer compared to 4.3% of the nonsmokers. Despite the small numbers the association between smoking and lung cancer is evident.

- 0501 DIFFERENTIAL CYTOLOGICAL AND CYTOCHEMICAL RESPONSES OF VARIOUS CULTURES FROM MOUSE TISSUES TO REPEATED EXPOSURES TO PUFFS FROM THE GAS PHASE OF CHARCOAL-FILTERED FRESH CIGARETTE SMOKE. (E.) Leuchtenberger, C. (Swiss Inst. Exp. Cancer Res., Lausanne) and R. Leuchtenberger. *Exp Cell Res* 62(1):161-172, 1970.

The morphological and cytochemical effect on DNA of repeated exposure to puffs of the gas phase from charcoal-filtered fresh cigarette smoke was studied in 3 types of primary cultures from mouse tissues (kidney tissue, embryonic lung organ, and lung explants) and in the 3T3 established cell line. Primary kidney tissue, embryonic lung organ, and lung explants (with outgrowing macrophages and epitheloid cells) were unaffected by the repeated exposures. The 3T3 cells were markedly stimulated by the puffs of the gas phase (independent of the puff volumes) with an enhancement of mitosis, cellular atypism (increase of DNA in interphase cells and metaphase chromosomes), tendency to nuclear fusion, and piling up of cells, but no morphological cell transformation was observed.

- 0502 RAT GASTRIC SECRETION AND MUCOSAL SEROTONIN FOLLOWING CHRONIC ORAL NICOTINE INTGESTION. (E.) Thompson, J. H. (U. California Los Angeles Sch. Med.), M. Angulo and C. A. Spezia. *Res Commun Chem Path Pharmacol* 1(6):721-732, 1970.

Gastric secretion (ml/100 g) and gastric mucosal serotonin ($\mu\text{g}/\text{tissue}$) were measured in 2-hr pylorus-ligated Sprague-Dawley rats after 2 weeks of exposure to nicotine (100 $\mu\text{g}/\text{kg}/\text{day}$ or 1000 $\mu\text{g}/\text{kg}/\text{day}$) in drinking water with and without atropine (100 $\mu\text{g}/\text{kg}$, s.c.) injected during ligation. Nicotine (1000 $\mu\text{g}/\text{kg}/\text{day}$) significantly increased gastric secretion (0.4 to 0.95) while atropine reduced gastric secretion in both controls and nicotine-treated animals

to 0.1. Total gastric mucosal serotonin dropped from the control level of 2.44 to 2.03 with the lower dose of nicotine and to 1.74 with the higher dose; atropine slightly reduced the serotonin levels of each group (2.28, 1.74, and 1.46, resp.). The increase in gastric secretion and depletion of mucosal serotonin may be related.

- 0503 CYTOGENETIC STUDIES ON WOMEN USING ORAL CONTRACEPTIVES AND THEIR PROGENY. (E.) McQuarrie, H. G. (Gynec. Obstet. Clin. Inc., Salt Lake City, Utah), C. D. Scott, H. S. Ellsworth, J. W. Harris and R. A. Stone. *Amer J Obstet Gynec* 108(4):659-665, 1970.

Users of oral contraceptives and children of users of oral contraceptives were subjected to cytogenetic studies. Subjects included 50 babies born to mothers after oral contraceptive use (sequential mestranol and mestranol with chlormadinone), 23 women using oral contraceptives (mestranol or norethindrone), and 20 women who reportedly had never used oral contraceptives. Dermatoglyphic studies were also performed on the babies. One baby had D/G translocation Mongolism. In the oral contraceptive users, increased chromosome breakage and satellite association were observed. Such abnormalities were more frequent in contraceptive users than in non-users (18 users and 7 non-users had breaks).

- 0504 CERVICAL CYTOLOGY AND SEQUENTIAL BIRTH CONTROL PILLS. (E.) Dougherty, C. M. (Louisiana St. U. Med. Ctr., New Orleans). *Obstet Gynec* 36(5):741-744, 1970.

The correlation of cytological abnormalities, possibly associated with carcinoma *in situ* of the cervix, and sequential contraceptive pills was studied in 1983 women. Initial cytologic smears were negative in 1933 of these women and positive in 50 women (cervical carcinoma in 15 cases and atypical epithelial hyperplasia in 35 cases). The incidence of cytologic abnormalities was observed at various periods after commencement of a course of oral contraceptives, with the result that after 14-26 menstrual cycles on the sequential contraceptive pills, 1021 women showed negative smears, 16 showed atypical and 7 showed positive smears. This finding yields a rate of atypical and positive smears/1000 cycle of 15 and 7, resp., after 14-26 cycles. The results indicated that the observed rate of occurrence of cytologic abnormalities in patients on contraceptive pills was about twice as high as the rate expected in control subjects. None of the patients studied developed mammary carcinomas, adenocarcinomas or stromal sarcomas, but 7 benign mammary masses were found.

- 0505 THE EFFECT OF ORAL CONTRACEPTIVES ON THE HISTOLOGY OF CARCINOMA OF THE BREAST. (E.) Penman, H. G. (U. Otago Med. Sch., Dunedin, New Zealand). *J Path* 101(1):66-68, 1970.

The histological appearance of a malignant tumor in the breast of a woman who had been taking oral con-

traceptives was examined. The patient, a 27 yr-old mother of 2, had used 3 different brands of birth control pills for 3 yr when she developed a tumor in her right breast. Mastectomy was performed, and the tumor was diagnosed as an extensively infiltrating type of comedocarcinoma. The intraduct portion of the tumor displayed prominent "colostrum corpuscles", and there were metastases to the lymph nodes which were composed of markedly eosinophilic cells. The occurrence of colostrum-like foamy cells in the cytoplasm of the tumor cells appears to agree with the suggestion that these cells are associated with hyperplastic disorders correlated with hormonal disturbances of the type brought on by oral contraceptives.

- 0506 A PATIENT WITH A METASTASIZED OVARIAN CARCINOMA, CURED (?) AFTER CYTOSTATIC TREATMENT; DEATH FROM ACUTE MYELOGENIC LEUKEMIA. (Dut.) Smit, C. G. S. (Diakonessen Hosp., Groningen, Netherlands) and L. Meyler. *Nederl T Geneesk* 114 (39):1620-1623, 1970.

Death from acute myelogenous leukemia of a 44-yr-old woman who had received extensive cytostatic treatment for bilateral ovarian papilliferous cystadenomata (which had metastasized to the peritoneum and to the omentum is reported. The patient underwent resection of the cystadenomata and of the omentum and was treated with cyclophosphamide (50 mg 3 x daily for 24 months) and x-ray therapy for 3 months (9000 r); 2 yr after the resection, she was free of metastases. However, 2 yr later a second laparotomy revealed an inoperable tumor in the pelvic cavity, and carcinomatous metastases were found in the peritoneum similar to those excised 4 yr earlier. Treatment with thiotepea was commenced (15 mg/wk), and 11 months after the laparotomy, the metastases seemed to have disappeared. However, anemia, thrombopenia and leukopenia were now observed, and the patient died from acute myelogenous leukemia.

- 0507 MULTIPLE MYELOMA AND ACUTE MYELOMONOCYTIC LEUKEMIA: REPORT OF FOUR CASES POSSIBLY RELATED TO MELPHALAN. (E.) Kyle, R. A. (Mayo Clin., Rochester, Minn.), R. V. Pierre and E. D. Bayrd. *New Eng J Med* 283(21):1121-1125, 1970.

Four patients, 1 suffering from a plasma-cell dyscrasia with systemic amyloidosis, and 3 suffering from typical multiple myeloma involving anemia, elevated sedimentation rate, monoclonal serum peak, Bence-Jones protein in the urine, lytic bone lesions, and increased myeloma cell counts in the marrow, were treated with melphalan (L-phenylalanine mustard) for periods of 30-57 months; all 4 patients developed acute myelomonocytic leukemias of rapid progression. The remote likelihood of chance association of acute leukemia and multiple myeloma (the probability of leukemia occurring in 250 cases of myeloma is 1:50,000), the known effect of alkylating agents on DNA, the fact that the leukemia was myelomonocytic, and the long period of treatment with melphalan all suggest that melphalan therapy played an etiologic role in the development of leukemia in these cases.

- 0508 LYMPHOCYTE TRANSFORMATION OBSERVED IN SULFAMYLON AGRANULOCYTOSIS. (E.) Maurel L. H. (Dartmouth Med. Sch., Hanover, N. H.), P. Andrews, F. Rueckert and O. R. McIntyre. *Plast Reconstr Surg* 46(5):458-462, 1970.

DNA synthesis (^3H -thymidine incorporation) in the lymphocytes of a patient who had developed Sulfamylon agranulocytosis during treatment with Sulfamylon cream (α -amino-p-toluenesulfonamide) and in lymphocytes of 4 control subjects (2 normal and 2 hospitalized patients treated with Sulfamylon cream for longer than a month) was measured in the presence of Sulfamylon acetate (1 mg%) or its major metabolite, sulfamylbenzoic acid (1 mg%). ^3H -Thymidine incorporation (cpm) was 2.5 times greater with sulfamylbenzoic acid (592) than in its absence (232) in the lymphocytes of the patient who had agranulocytosis although Sulfamylon (200) had not affected the incorporation. Lymphocyte transformation did not occur with either Sulfamylon or its metabolite in the 2 normal subjects or in the other control patients.

- 0509 A CASE OF LEUKEMIA FOLLOWING EXPOSURE TO INSECTICIDE. (E.) Hoshizaki, H. (Osaka Red Cross Hosp., Japan), Y. Niki, H. Tajima, Y. Terada and A. Kasahara. *Acta Haemat Jap* 32(4):672-677, 1970.

A case report of a Japanese sanitation employee with acute leukemia apparently associated with occupational exposure to the insecticides benzene hexachloride and chlorophenothane (DDT) is described. In the course of his work, the patient, a 44-yr-old male, sprayed these agents on houses and into sewers. He neglected to wear a face mask and probably inhaled the insecticides over the 8-yr period of his employment. On autopsy, abundant hemosiderin was found in each organ, especially in the liver, spleen and lymph nodes; no infiltration of leukemic cells into the liver and spleen was observed. The final diagnosis was acute leukemia with hypoplastic marrow and hemosiderosis. Possibly, exposure and resorption of chlorophenothane and benzene hexachloride via the alveoli led to aplastic anemia which then transformed into acute leukemia.

- 0510 NICKEL CARBONYL POISONING: REPORT OF TWO CASES. (E.) Vuopala, U. (Dept. Med. U. Oulu, Finland), E. Huhti, J. Takkunen and M. Huhti. *Ann Clin Res* 2(3):214-222, 1970.

The symptomatic effects of nickel carbonyl gas exposure on 25 industrial workers were observed; nickel carbonyl gas is a lethal poison and putative carcinogen. All patients had temporary or continuous dyspnea, and most had a persistent feeling of fatigue and weakness, especially ocular weakness. Nausea, cough, liver tenderness, and toxic pneumonitis were other common symptoms. Laboratory studies showed that the nickel content in the urine of patients, initially elevated as high as 900-1000 mg/l, returned to normal levels (less than 100 mg/l) by 1 wk after exposure to nickel carbonyl gas. In 2 of the patients died, and in all cases symptoms

emitted in time. Any bearing of acute poisoning on carcinogenesis seen with chronic inhalation of nickel carbonyl remains to be established.

- 511 CLINICAL STUDIES ON TUMOR OF THE URINARY BLADDER: I. STATISTICAL AND CLINICAL STUDIES ON TUMOR OF THE URINARY BLADDER. (*Jap.*) Kajima, E. (Nara Med. U., Japan), T. Hiramatsu, Y. Motomiya, K. Iriya, I. Hayashi and M. Ishikawa. *Exp J Urol* 61(8):783-804, 1970.

marked male predominance was observed in 150 cases of primary urinary bladder tumor studied at Nara Medical University, Japan, with 126 of the patients being male. The age distribution of the patients with urinary bladder tumors ranged from 3-84 yr, and the maximum incidence occurred in the 5th decade of both sexes. Occupational distribution of 89 patients with urinary bladder cancer revealed a remarkably frequent occurrence in workers in agriculture and forestry. One patient had been exposed to aniline dyes for 7 yr. A correlation between cigarette smoking and the development of urinary bladder tumors was significant in the present studies. In males, 47 patients (90.2%) of 52 cases and 71 patients (72.4%) of 98 controls were smokers. In females, 7 patients (63.3%) of 11 cases and 9 patients (16.7%) of 54 controls were smokers. Single tumors of the urinary bladder were noticed in 93 of 150 patients (62.0%). Fifty of 93 tumors (53.8%) were located on the lateral wall, 19 (20.4%) in the trigone, 9 (9.7%) on the posttrigone, 8 (8.6%) in the bladder neck, 6 (6.4%) on the vault, and 1 (1.1%) on the anterior wall. In 96 of 98 cases receiving histological classification, tumors were found to be transitional cell papilloma and carcinoma. The 5-yr survival rate, dated from the onset of symptoms, was zero in untreated cases, 50% in patients treated with suprapubic excision of tumors.

- 512 SODIUM CYCLAMATE AND BLADDER CARCINOMA. (*E.*) Brower, L. P. (Dept. Biol., Amherst Coll., Mass.). *Science* 170(3957):558, 1970.

- 513 OBSERVATIONS ON THE REGULATION OF CHEMICAL INTAKE IN CHRONIC CARCINOGENESIS STUDIES. (*E.*) Toth, B. (U. Nebraska Coll. Med., Omaha) and J. Shubik. *Food Cosmet Toxic* 8(3):297-299, 1970.

- 514 USE OF CONTRACEPTIVES: CERVICAL-UTERINE EPITHELIAL ATYPIAS. (*Sp.*) Nogales Fernandez, F. (Fac. Med. Madrid, Spain) and A. Tarancon Martinez. *Acta Gynec* 21(9):649-658, 1970.

- 515 ON POLLUTION OF RESERVOIRS BY CARCINOGENIC HYDROCARBONS. (*Rus.*) Il'nitskly, A. P. (USSR Acad. Med. Sci., Moscow) and L. G. Rozhkova. *Op Onkol* 16(7):78-82, 1970.

- 0516 ON THE ACTIVE PRINCIPLES OF CROTON OIL: X. PREPARATION OF TRITIUM LABELED CROTON OIL FACTOR A₁ AND OTHER TRITIUM LABELED PHORBOL DERIVATIVES. (*E.*) Kreibich, G. (German Cancer Res. Ctr., Heidelberg) and E. Hecker. *Z Krebsforsch* 74(4):448-456, 1970.

- 0517 ACUTE TOXICITY OF AFLATOXIN B₁ IN HAMSTERS. (*Fr.*) Santiago, M. (no affil) and C. Besucchio. *Arch Anat Path* 18(3):229, 1970.

- 0518 CONTROL OF CHEMICAL POLLUTANTS. (*E.*) Epstein, S. S. (Harvard Med. Sch., Boston, Mass.). *Nature* 228(5274):816-819, 1970.

- 0519 AFLATOXIN PRODUCTION AS AFFECTED BY ENVIRONMENTAL CONSIDERATIONS. (*E.*) Epstein, E. (Dept. Food Sci., U. Illinois, Urbana), M. P. Steinberg, A. I. Nelson and L. S. Wei. *J Food Sci* 35(4):389-391, 1970.

- 0520 CARCINOGENIC POTENCY, "SUPERDISLOCABILITY INDEX" AND CHEMICAL DISPLACEMENTS IN DIBENZACRIDINES AND DIBENZANTHRACENES. (*Fr.*) Clin, B. (Fac. Sci. Gironde, France) and B. Salier. *C R Acad Sci* 271(10):858-861, 1970.

See also:

- * (Rev): 0346, 0347, 0348, 0361, 0367, 0376, 0378, 0383, 0386, 0387, 0388
- * (Viral): 0653
- * (Immun): 0693, 0695, 0726
- * (Epid-Biom): 0751
- * (Misc): 0815

- 0521 CHROMOSOME AND CHROMATID-TYPE ABERRATIONS INDUCED BY COBALT⁶⁰ IRRADIATION AND TRITIATED URIDINE IN HUMAN LEUKOCYTE CULTURES. (E.) Lindahl-Kiessling, K. (Inst. Med. Genet. Zoophysiology, U. Uppsala, Sweden), B. Santesson and J. A. Book. *Chromosoma* 31(3):280-284, 1970.

Cobalt⁶⁰ irradiation and ³H-uridine irradiation were administered to cultures of human leucocytes in order to observe the chromosome and chromatid-type aberrations induced by this treatment; phytohemagglutinin was added to cultures after one exposure to ⁶⁰Cobalt (200-600 rads every hr) or ³H-uridine irradiation (30 µC/ml) of medium. Irradiated cells were collected at the time of their first mitotic event. In the cultures treated with ³H-uridine mainly breaks of chromatid type were found (129 chromatid aberrations/1461 cells analyzed), whereas the ⁶⁰Co irradiated cells have only breaks of chromosome type as long as the irradiation takes place before the onset of DNA synthesis (73 cells with chromosome aberrations, maximum and 9 with chromatid aberration, maximum). Apparently, ³H-uridine damages localized single stranded DNA loops separated during transcription in RNA synthesis and which are inaccessible to repairing. The results seem to indicate that the subunit of the chromosome as revealed by radiation is single-stranded DNA, and that the chromosome or chromatid continuity depends on 1 DNA double helix strand.

- 0522 EFFECT OF γ-RAYS ON INFECTIVITY AND CAPACITY FOR NUCLEAR-ASSOCIATED AND CYTOPLASMIC DNA REPLICATION OF FV3 IN CHICK EMBRYO FIBROBLASTS. (E.) Aubertin, A. M. (I. N. S. E. R. M., Strasbourg, France), C. Decker and A. Kirn. *Radiat Res* 44(1):178-180, 1970.

Frog virus 3 was grown in chick embryo fibroblast culture, and irradiated with γ-rays produced by ⁶⁰Co irradiation at a rate of 600 rads/min in order to investigate the effect of γ-rays on the virus' ability to infect and to replicate nuclear and cytoplasmic DNA. γ-Rays produced a dissociation of the capacities for infectivity, nuclear-associated DNA replication, and cytoplasmic DNA replication. When the amount of DNA synthesis induced by irradiated virus was expressed as a percentage of that induced by nonirradiated virus, the inactivation of the capacity for DNA replication (nuclear as well as cytoplasmic fraction) followed a simple exponential law. The rate of inactivation by γ-rays of the capacity for nuclear-associated DNA replication (37% inactivation dose was 8×10^5 rads) was half that of the capacity for cytoplasmic DNA replication (37% inactivation dose was 4×10^5 rads). This indicates that the synthesis of DNA which appears in the cytoplasm required more cistrons than the synthesis of the nuclear-associated DNA, and that the passage from cytoplasmic DNA to the virions required further protein synthesis. The capacity of frog virus 3 to inhibit host-cell DNA replication was not affected by γ-rays.

- 0523 DOUBLE-STRAND BREAKS IN THE DNA OF A MURINE LYMPHOMA CELL AFTER X-IRRADIATION. (E.) Lehmann, A. R. (Roy. Cancer Hosp. Lab., Belmont, Surrey, England) and M. G. Ormerod. *Biochem Biophys Acta* 217(2):268-277, 1970.

Double-stranded DNA scissions produced by X-irradiation of murine lymphoma cells were studied by measuring the molecular wt of the DNA of irradiated cells. Murine lymphoma cells (strain L5178Y) were labeled with tritiated thymidine, exposed to 220 kV X-rays and lysed on neutral sucrose gradients; the molecular wt of the released DNA was measured by rate of sedimentation through the gradients. Only when the speed of centrifugation was less than 20,000 rpm was sedimenting DNA pure and unaggregated, and at this speed did the sedimentation of the DNA truly reflect its molecular wt. Double-strand breaks were formed in the DNA of murine lymphoma cells as single events with an efficiency of 2900 ± 400 eV/break. After X-ray doses of more than 20 krad, these breaks were not rejoined on post-irradiation incubation. The molecular wt of DNA from unirradiated cells was at least 3×10^9 ; DNA molecules of molecular wt less than 10^9 were usually sedimented freely under appropriate conditions.

- 0524 THE RESPONSE OF STEM CELLS OF INTESTINAL MUCOSA TO IRRADIATION WITH 14 MeV NEUTRONS. (E.) Withers, H. R. (U. Texas M.D. Anderson Hospital, Tumor Inst., Houston), J. T. Brennan and M. M. Brenner. *Brit J Radiol* 43(515):796-801, 1970.

The survival and damage-repair reactions of jejunal crypt cells of female mice exposed to whole-body X-ray- and neutron-irradiation were studied. Mice were subjected to doses of 100-135 rads of 200 kV X-radiation or 82-142 rads of 14 MeV neutrons, and the survival and repair of crypt cells in the intestinal mucosa were assayed. Slopes of dose survival curves for X-ray- and neutron-irradiation were similar, the shoulder on the neutron curve being narrower than the shoulder of the X-ray curve with 10^2 clonogenic cells surviving 675 rads of X-ray irradiation and $10^{3.3}$ clonogenic cells surviving a comparable dose of X-rays. Neutron-irradiated cells repaired less sublethal injury than X-ray-irradiated cells. However, the repair observed between doses of 14 MeV neutrons was greater than repairs observed with neutron-irradiation at lower energies.

- 0525 PATHOGENESIS OF RADIATION-INDUCED DYSPLASIA. (E.) Shively, J. N. (Col. Vet. Med. Biol. Sci., Colorado St. U., Fort Collins), R. D. Phemister, G. P. Epling and R. Jensen. *Invest Ophthalmol* 9(11):888-900, 1970.

The response of the developing retina of 2-day-old beagle dogs to γ-irradiation (170 r) and the pathogenesis of associated retinal dysplasia were followed with light and electron microscopic observation over periods ranging from 1 hr to 180 days postirradiation. One hr after irradiation an onset of degenerating and pyknotic cells were observed in the vitreal part of the neuroblastic layer and

the inner nuclear layer; after 12 hr 10-20% of the cells had become pyknotic. After 1 and 2 days necrosis was more widespread in the posterior section of the retina and ectopic cells were seen, while after 4 days necrosis became less prominent until after 8-10 days postirradiation dysplasia was evident. The most conspicuous manifestations of the dysplasia (rosettes, tubules, and nests of ectopic photoreceptor cells) persisted for 180 days when atrophy of the dysplastic areas was noted.

0526 INCORPORATION OF ^{14}C - AND ^3H -THYMIDINE IN LYMPHOCYTES AFTER EXTRACORPOREAL IRRADIATION OF THE BLOOD. (E.) Rosengren, B. (Sahlgrenska sp., Goteborg, Sweden), S. E. Bergentz, K. Nordahl-Kiessling, L. Lindholm and B. Persson. *Rev Trop Etud Clin Biol* 15(7):778-782, 1970.

The effect of extracorporeal irradiation on the capacity of human lymphocytes to synthesize DNA following phytohemagglutinin stimulation or allogenic lymphocyte stimulation was investigated. Blood samples were collected from patients after extracorporeal radiation of the blood via an arteriovenous shunt dialysis tubing (multiple doses totaling 12,000-40,000 rads), and cells were stimulated by the addition of phytohemagglutinin or allogenic cells to cultures. DNA synthesis was assayed by allowing the incorporation by the lymphocytes of ^3H -thymidine or ^{14}C -thymidine. Incorporation of ^3H -thymidine by phytohemagglutinin-stimulated cultures was reduced by irradiation; ^{14}C -thymidine activity was 1,800 cpm in 1 patient 16 hr after blood irradiation with 18,000 rads and 202 cpm 21 hr after 20,000 rads. Reduced capacity to incorporate ^3H -thymidine following irradiation without phytohemagglutinin stimulation was also noted in lymphocytes of patients whose capacity to incorporate the label was measured before and after treatment; in 1 such patient, thymidine incorporation before treatment with 4000 rads was measured to be 1.34×10^6 cpm and after treatment was 3.75×10^5 cpm. Reduction of label incorporation consequent to irradiation was especially evident immediately after irradiation; and variations in the response to irradiation among different patients may have been due to variations in the exchange between circulating and noncirculating lymphocytes.

0527 CHROMOSOME ABERRATIONS INDUCED BY AN ULTRASONIC FETAL PULSE DETECTOR. (E.) Macintosh, I. J. C. (Med. Sch., U. Cape Town, Union of South Africa) and D. A. Davey. *Brit Med J* 4(5727):1-93, 1970.

Vessels containing 5 ml of blood cultures from healthy humans were exposed to ultrasound produced by an ultrasonic fetal heart detector for periods of 1 and 2 hr; the culture in one vessel was permitted to form standing waves produced by ultrasound, but standing waves were suppressed by polyethylene membranes in the second culture vessel. The ultrasound treatment produced a marked and consistent rise in the number of blood culture cells with chromosomal aberrations; cells in the vessels

exposed to ultrasound for varying periods exhibited cell-aberration totals of 26, 50, and 22 aberrations/100 cells as compared to 5 aberrations/100 cells recorded for untreated controls. The vessel showing the highest number of aberrant cells/100 had been the one exposed to ultrasound for 2 hr and in which standing waves had been eliminated.

0528 LATE GASTRIC CARCINOMA DEVELOPING AFTER SURGERY FOR BENIGN CONDITIONS: ENDOSCOPIC AND HISTOLOGIC STUDIES OF THE ANASTOMOSIS AND DIAGNOSTIC PROBLEMS. (E.) Kirsner, J. B. (U. Chicago Dept. Med., Ill.), S. Kobayashi and J. C. Prolla. *Amer J Dig Dis* 15(10):905-912, 1970.

Seven patients who underwent surgery for benign gastroduodenal diseases (including duodenal and gastric ulcers) developed gastric carcinomas after a mean elapsed time of 23 yr since the original operation. Surgical operations performed included Billroth operations I and II and gastroenterostomy. In all 7 cases, the carcinomas involved the anastomotic area; gastroscopic biopsy demonstrated a high incidence of atrophic gastritis and frequent polypoid formation at or near the anastomotic site. More patients who underwent gastrojejunectomy than the Billroth I operation exhibited these changes. Although the frequent occurrence of gastric atrophy with intestinal metaplasia has suggested a close relationship between the development of carcinoma and anastomosis with gastroenterostomy, endoscopic and biopsy studies did not demonstrate progressive advancement of gastric atrophy.

0529 THYROID NEOPLASIA AS LATE EFFECT OF EXPOSURE TO RADIOACTIVE IODINE IN FALLOUT. (E.) Conard, R. A. (Brookhaven Natl. Lab., Upton, N.Y.), B. M. Dobyns and W. W. Sutow. *JAMA* 214(2):316-324, 1970.

The development of thyroid neoplasia in inhabitants of Rongelap Island, who were accidentally exposed to radioactive iodine as bomb-fallout in 1954 (doses of 69-175 rad) was investigated in yearly checkups. Thyroid abnormalities had developed in 21 of 67 of these people, 3 with malignant lesions, 16 with benign adenomatous nodules, and 2 with atrophy of the gland with hypothyroidism. The preponderance of lesions occurred in children exposed at less than 10 years of age who had received a greater thyroid exposure. Growth retardation associated with hypothyroid tendency was noted in some children who appear to be responding favorably to thyroid hormone medication. Apparently, exposure to radioactive iodine and exposure to x-irradiation carry approximately the same risk of thyroid cancer.

0530 THE MALIGNANCY OF MIXED TUMORS OF THE PAROTID GLAND: A CLINICOPATHOLOGICAL ANALYSIS OF 70 CASES. (E.) Saksela, E. (3rd Dept. Path., U. Helsinki, Finland), J. Tarkkanen and A. Kohonen. *Acta Otolaryng* 70(1):62-70, 1970.

Tumor tissue from 119 cases of parotid tumor was subjected to histopathological classification

related to the clinical history of the condition and to the findings of 5 yr follow-up data; tumors studied included benign "mixed tumor" (the most common finding, accounting for 64 of the 119 cases) and carcinoma in mixed tumor (6 cases). Only carcinoma in mixed tumor behaved in a malignant fashion and the rest of mixed tumors showed a benign course of disease. The number of recurrences was higher in the group of tumors with multiple nodules, and otherwise no differences in the behavior was noted as related to cellularity, cell atypism and mitotic frequency. Of the 6 patients with carcinoma in mixed tumor 3 had received irradiation therapy (3000-6000 rads) for a parotid tumor not surgically removed 8-24 yr prior to present rapid enlargement. None of the patients with equally long histories of benign mixed tumors had received irradiation treatment.

0531 MULTIPLE BASAL CELL CARCINOMAS ARISING IN RADIATED BURN SCARS: CASE REPORT. (E.)

Stone, N. H. (Chicago Med. Sch., Ill.) and M. M. Montiel. *Plast Reconstr Surg* 46(5):506-509, 1970.

The case of an Australian woman who was severely burned in childhood, and received protracted radiation therapy to relieve keloid formations developing on the burn scars is reported. Twenty-two yr later, the patient presented with multiple basal cell carcinomas on skin areas which had been both burned and irradiated, including abdomen, groins, lower thorax and anterior thighs. Only those areas which had been both burned and irradiated showed lesions, a feature of the case which may suggest that burns and irradiation acted as co-carcinogens.

0532 MALIGNANT TUMORS OF THE RAT ADRENAL GLAND INDUCED BY FISSION NEUTRON IRRADIATION. (E.)

Vogel, H. H., Jr. (Coll. Med., U. Tennessee, Memphis) and R. Zaldivar. *Int J Radiat Biol* 18(3):267-270, 1970.

Adrenal carcinomas were found in rats that were subjected to whole-body fission neutron irradiation when 6-10-wk-old; histological studies revealed that the neoplasms were cortical carcinomas and in 1 case pleomorphic sarcoma. Only 1.1% of the control rats not receiving irradiation developed such tumors compared to a 13.1% incidence in irradiated rats. The tumors showed cytological signs of malignancy and lacked a fibrous capsule surrounding the tumor; tumor-cell emboli were found in the blood vessels of affected rats, and metastasis to the intestine was observed. The pleomorphic sarcoma of the adrenal was a relatively large tumor exhibiting a considerable amount of necrosis and showing a variety of highly malignant cell-types. The radiation-induced tumors represented late radiation effects, with age at death ranging from 414-1311 days.

0533 RECOVERY FROM RADIATION INJURY WITH AND WITHOUT BONE MARROW TRANSPLANTATION: EFFECTS OF SPLENECTOMY. (E.)

Smith, L. H. (Oak Ridge Natl. Lab., Tenn.) and T. W. McKinley, Jr. *Radiat Res* 44(1):248-261, 1970.

The effect of lethal X-irradiation on splenectomized mice which had been injected with syngeneic bone marrow was investigated, in order to assess the importance of the spleen for recovery from radiation injury. Mice were splenectomized at different times before exposure to 650-950 rads of X-irradiation; bone marrow was usually injected 4 hr after irradiation. Splenectomy 2 days prior to irradiation of mice not injected with marrow cells improved the 30-day survival of irradiated mice, especially in the 750-850 rad range, with 95% of splenectomized mice surviving 750 rads, and 50% of intact mice surviving the same dose. The protective effect of splenectomy performed 2 days before irradiation was higher (71% survival) than the protective effect of splenectomy performed 30 days before irradiation (44% survival). Injection of bone marrow in splenectomized and unsplenectomized mice had the effect of equalizing 30-day survival rates for both groups of animals. Splenectomy performed after irradiation reduced survival, and survival varied inversely with the interval between marrow injection and splenectomy. Ferrokinetic studies using ^{59}Fe indicated that in lethally irradiated mice injected with marrow cells early regenerative erythropoiesis was reduced in those animals splenectomized prior to irradiation but only when the dose of marrow cells was limiting. Apparently, the spleen contributes to the early restoration of a hematopoietic compartment least critical to the survival of the animal; whatever contribution the spleen makes to survival is compensated for by other tissues when the spleen is absent. Splenectomy 2 days before irradiation increased the irradiation $\text{LD}_{50/30}$ by approximately 65 rads, a protective effect which remains unclear.

0534 BONE MARROW AND SPLEEN INTERRELATION IN LOCAL IRRADIATION: DATA OF CYTOMETRY

Fe^{59} INCORPORATION. (E.) Kabakov, Y. N. (USSR Acad. Med. Sci., Obninsk) and K. A. Folanova. *Folia Haemat* 94(1):64-73, 1970.

Cytometric studies and studies of Fe^{59} incorporation were performed on lymphocytes from irradiated bone marrow and spleen of rats. Lymphocytes from the spleen of rats which had been exposed to 1000 rads of X-irradiation were subjected to cytometric measurement, and Fe^{59} incorporation by cells of locally irradiated and screened bone marrow was terminated in a separate group of animals. Cytometric examination from 0-10 days after irradiation showed that lymphocytes of the spleen, locally irradiated and screened bone marrow had diameters of 6-15 μm with 9 μm being the prevailing size in both spleen and bone marrow. Numbers of small lymphocytes (diameters less than 9 μm) decreased significantly (50% decrease) coincidentally with the intensive restoration of erythropoiesis in the locally irradiated region and with the increase in numbers of normoblasts. Fe^{59} incorporation also showed a negative correlation with recovery of irradiated bone marrow and with restored stability of erythropoiesis in screened bone marrow. Immediately prior to recovery of locally irradiated bone marrow, a significant decrease in the distribution of spleen

lymphocytes was noted. Apparently, small lymphocytes may participate in the recovery of irradiated bone marrow as precursor cells capable of accelerated transformation into normoblasts.

- 0535 OSTEOSARCOMA AND PAROSTEAL SARCOMA OF THE MAXILLA AND MANDIBLE: STUDY OF 20 CASES. (E.) Roca, A. N. (U. Texas Med. Branch, Galveston), L. Smith, Jr. and B. S. Jing. *Amer J Clin Path* 44(4):625-636, 1970.

The pathology and incidence of osteosarcoma and parosteal sarcoma of the maxilla and mandible were studied in a series of 20 cases. Nine tumors were located on the maxilla, 11 on the mandible. The average age of patients with maxillary sarcoma was 35.6 yr, and the average age of patients with mandibular sarcoma was 50.4 yr. The patients comprised 13 men and 7 women; 15 patients were Caucasian. None of the patients had a previous history of trauma, Paget's disease or benign bone tumors, although 2 osteosarcomas arose in patients who had been irradiated. The average age of onset for osteosarcoma of the jaw was 1 or 2 decades later, than the average age of onset for osteosarcomas of other regions. Gross features of parosteal osteosarcoma included a regular external surface without a cartilaginous cap. Tumors were primarily composed of intermixed bone and fibrous and cartilaginous tissue. Microscopically, tumors showed abundant calcification and anaplastic osteoblasts with proliferation of malignant osteoblasts and osteoid production. Osteosarcomas exhibited a greater tendency to metastasize than did parosteal osteogenic sarcoma.

- 0536 ACTION SPECTRUM OF ULTRAVIOLET LIGHT-INDUCED DAMAGE TO NUCLEAR DNA *IN VIVO*. (E.) Tan, E. M. (Scripps Clin., Res. Found., La Jolla, Calif.), R. G. Freeman and R. B. Stoughton. *J Invest Derm* 55(6):439-443, 1970.

The range of UV radiation capable of inducing damage *in vivo* to DNA in the epidermis of hairless mice was determined using an indirect immunofluorescent technique with antiserum against UV-irradiated DNA. UV radiation from 254 nm to 300 nm was effective in producing damaged DNA at energy levels (88-140 millijoules/cm²) comparable to 10 MED (human minimal erythema dose). At 305 nm 10 MED was sufficient to produce photochemical lesions, but they were not as extensive as those produced at the shorter wavelengths. At 310 and 320 nm, 7,200 millijoules/cm² of energy was required to produce the nuclear lesions, while at 330 nm no lesions were evident even with this high energy.

- 0537 THE METABOLISM OF ISOLATED PERFUSED RAT LIVER FOLLOWING *IN VITRO* RADIATION. (Ger.) Stähler, F. (Inst. Biophys. Radiobiol., U. Hamburg, Germany) and I. Sinn. *Strahlentherapie* 140(2):213-220, 1970.

Changes in the content of free amino acids in rat liver following irradiation with X-rays were inves-

tigated in order to determine the role of the liver as a regulating organ in this context. The liver, isolated from healthy rats, was perfused with plasma with washed beef erythrocytes as oxygen carriers, and various amino acids as substrates. The irradiation doses were 1000 or 5000 rads (200 kV X-rays), and the amino acid content of the cytoplasm and of the perfusion fluid was followed for 3 hr. An altered amino acid metabolism in the *in vitro* preparation resulted following irradiation, but liver metabolism following whole body irradiation was relatively unchanged. The perfused liver changes were partly dose dependent; utilization of the incorporated amino acids following radiation at 1000 rad was increased, but this was decreased at the 5000 rad level, and on prolonged perfusion these values became equal. The intracellular amino acid content following 1000 rad was reduced. Tryptophan and arginine incorporation was decreased, and threonine elimination and taurine synthesis were stimulated. The mean quotient of the intra/extracellular amino acid content, which is directly related to the active transport of amino acids through the cell membrane, appeared to decrease with the irradiation dose.

- 0538 LONG-TERM CYTOGENETIC AND CLINICAL CONTROL OF A CHILD FOLLOWING INTRAUTERINE IRRADIATION. (E.) Kucerova, M. (Postgrad. Med. Inst., Prague, Czechoslovakia). *Acta Radiol* 9(4):353-361, 1970.

Cytogenetic studies were performed on a 4-yr-old child who had been exposed to roentgen irradiation *in utero* when its mother underwent radiation therapy (total of 3580 r) for cervical cancer. The child, a girl, exhibited mental retardation, microcephaly, and slight anemia and leucocytosis. Cytogenetically, the patient revealed a significant increase of mitoses with chromosome aberrations, the percentage of aberrant mitoses in the blood increasing from 6.6% in the first post-irradiation yr to 20% in the third postirradiation yr; a sharp increase in aberrant mitoses following irradiation had also been noticed in the mother (deceased at the time of the report). Both mother and child had increased incidence of monotrismy (an increase from 2% to 5.40% in the child in 4 yr) following irradiation exposure as well as increased chromosome breaks (an increase from 1.5% to 4.1% in 4 yr).

- 0539 RELATIVE BIOLOGICAL EFFECTIVENESS OF HEAVY IONS IN PRODUCING MUTATIONS, TUMORS, AND GROWTH INHIBITION IN THE CRUCIFER PLANT, *ARABIDOPSIS*. (E.) Hirono, Y. (Biol. Res. Lab., Nippon Soda Co., Kanagawa, Japan), H. H. Smith, J. T. Lyman, *Radiat Res* 44(1):204-223, 1970.

A heavy-ion linear accelerator was used to bombard dry seeds of the crucifer plant, *Arabidopsis thaliana* with ¹²C, ⁴He, ⁷Li, ¹⁶O, ²⁰Ne and ⁴⁰Ar ions in order to investigate the effectiveness of heavy ions in producing mutations, tumors and growth inhibition in the mature plants. The lowest dose of heavy ion

irradiation which produced tumors in 63% of plants was 4.8 kilorads for ^7Li ions; the highest dose of X-rays producing 63% tumor-bearing plants was 159 kilorads. Evaluation of the relative biological effectiveness (RBE) of irradiation with various ions for producing tumors indicated that ^7Li ions have the highest RBE of the ions tested. For growth inhibition and mutation, as well as for tumor development, the RBE of the various ions showed the same pattern consistently; at radiation doses of 18 KeV/ μ , the RBE was low, and at 72-174 KeV/ μ the RBE was maximal. Application of track segment analysis indicates that sensitive sites are multiple in number or complex in structure with effective thickness of a few Å to a few tens of Å, which approximates molecular bond distances as in DNA.

- 0540 CHILDHOOD CANCER IN RELATION TO PRENATAL EXPOSURE TO ATOMIC BOMB RADIATION. (E.) Jablon, S. (Japanese Natl. Inst. Hlth., Hiroshima) and H. Kato. *Lancet* 2(7681):1000-1003, 1970.

An examination of childhood cancer incidence among 1292 children exposed prenatally to radiation from nuclear bomb blasts in Hiroshima and Nagasaki, Japan, revealed that during the first 10 yr of life in the children studied only 1 died of leukemia, indicating that radiation exposure produced no significant excess in mortality in this population. These findings showed that the "extra" deaths produced/1 million person-rads of radiation numbered 5.2, a figure which appears to conflict with the estimate of 572 extra deaths/1 million person-rads produced by fetal irradiation in a study by Stewart and Kneale. The explanation of the divergence of these results is obscure; it may be that in Stewart and Kneale's study the population examined (children of women undergoing pelvic irradiation during pregnancy for medical reasons) was at an unusually high risk of developing cancer for reasons other than fetal irradiation.

- 0541 SMALLER G CHROMOSOMES IN THE BONE-MARROW CELLS OF HEAVILY IRRADIATED ATOMIC-BOMB SURVIVORS. (E.) Kamada, N. (Res. Inst. Nucl. Med. Biol., Hiroshima, Japan), T. Tsuchimoto and H. Uchino. *Lancet* 2(7678):880-881, 1970.

Seventy-four survivors of the atomic bomb explosions in Japan in 1945 were examined to observe the incidence of chromosomal aberrations in the bone marrow in this population. Four of 13 people who had been from 0-1000 m from the hypocenter of the explosions had a total of 7 types of stable chromosome abnormality; aberrations included smaller G chromosomes morphologically similar to the Philadelphia chromosome in chronic myelocytic leukemia. None of those who had been more than 1000 m had chromosome abnormalities. The 4 subjects with smaller G chromosomes all experienced moderate or severe radiation sickness after the explosion, but none had any evidence of leukemia. The cells with smaller G chromosomes appear to constitute a clone in the bone marrow of these survivors; the percentage of the small G chromosome phenomenon in this population was 10.9.

- 0542 EFFECT OF RADIATION ON LECITHIN METABOLISM, SURFACE ACTIVITY, AND COMPLIANCE OF RAT LUNG. (E.) Naimark, A. (Fac. Med., U. Manitoba, Winnipeg, Canada), D. Newman and D. H. Bowden. *Canad J Physiol Pharmacol* 48(10):685-694, 1970.

Lecithin metabolism and surface properties of the lungs of rats irradiated with ionizing radiation were investigated. Two-month-old rats received single doses of 3000 rads of roentgen radiation in the right hemithorax, 1-4 months after which exposed lungs were compared with contralateral shielded lungs, and with the lungs of non-irradiated controls. Four months after exposure, irradiated lungs did not differ in DNA content from controls but exhibited decreased lecithin content (8.0 mg/g fresh wt for controls vs 6.9 mg/g in treated animals), depressed incorporation of palmitate- ^{14}C into lecithin *in vitro* (8.25×10^3 cpm/mg for controls vs 5.1×10^3 cpm/mg for irradiated rats), a decrease in the percentage of palmitic acid in the lecithin fraction (60% for controls vs 51% for irradiated animals). Changes in other phospholipids were qualitatively similar. The stability of bubbles expressed from the cut surface of irradiated lungs decreased progressively with time, indicating impaired surface activity of the lung-lining layer. This was associated with a progressive decrease in compliance of the lung. Electron microscopy revealed no qualitative changes in the alveolar epithelial cells. Morphologic evidence of injury was most prominent in the capillaries and could be detected before changes in phospholipid content, surface activity, and compliance; these changes consisted of swollen basement membranes, cytoplasmic vacuolation of the endothelial cells and occasional aggregates of platelets in the vessels. These findings appear to indicate that the changes in lecithin content and surface activity produced by irradiation of the lung were secondary to endothelial damage.

- 0543 RADIATION-INDUCED OSTEOSARCOMA IN THE RAT AS A MODEL FOR OSTEOSARCOMA IN MAN. (E.) Cobb, L. M. (Roy. Cancer Hosp., London, England). *Brit J Cancer* 24(2):294-299, 1970.

The pathology of experimentally-induced osteosarcoma (insertion of ^{32}P -impregnated polyvinyl chloride discs into the distal femoral metaphysis) in female Chester Beatty random-bred rats was compared with that of the spontaneous osteosarcoma in man. Discs with a surface dose rate of 27.6 r/min in tissue equivalent material produced osteosarcoma in 26 (28%) 6-14 months after implantation, and discs with a surface dose rate of 3.6 r/min caused the tumor in 1 rat (1%) 8 months after implantation. The tumors were identified by palpation at diameters of 1.5-2 cm and grew to 5-7 cm within 8 wk causing impairment of the animals' movements. Histopathologically the tumor in the rat is similar to osteosarcomata in man except that well-differentiated malignant osteoblasts predominate in the rat while cellular pleomorphism is found in man. Repeated transplantation of the rat osteosarcomata produced this cellular pleomorphism commonly seen in man.

- 0544 HORMONE-MEDIATED CHANGES OF LIVER POLY-RIBOSOMES IN IRRADIATED RATS. (E.)
 aeysens, W. (Ctr. Study Nucl. Energy, Mol, Belgium),
 Goutier and V. Vangheel. *Strahlentherapie* 140(2):
 04-212, 1970.

Liver polyribosomes in X-irradiated rats (500-2000 r) were compared (*in vitro* synthetic activity) with those of non-irradiated animals and the role of hormones in the mechanism for polyribosome modification was examined. In the presence of optimal amounts of cell sap (polysomal protein to cell sap protein ratio of 1:20) irradiated polysomes (500 r) incorporated more ^{14}C -phenylalanine than control polysomes; the increase in amino acid incorporation was proportional to the amount of irradiated polysomes used. Increasing the doses of irradiation increased the difference in incorporation between the irradiated group and the controls to over 30% after 1000 or 2000 r. Polyuridylic acid stimulated ^{14}C -phenylalanine uptake in polysomes from irradiated livers less (115%) than in polysomes from normal livers (175%). Local irradiation of the liver did not affect polysome distribution (sucrose density gradient), but whole-body irradiation with shielded liver shifted polysomes to heavier aggregates, and ACTH (10-12 U/100 g) produced a similar effect. Bilateral adrenalectomy did not interfere with the radiation-induced shift, but this negative result was due to the presence of accessory adrenal tissues in Wistar rats. The shift to a higher proportion of heavy polysomes may be a late result of the first stress reaction and may occur through stimulation of the hypothalamus-pituitary-adrenal axis.

- 0545 INDUCED CELL PROLIFERATION AND THE INITIATION OF SKIN TUMOR FORMATION IN MICE BY ULTRAVIOLET LIGHT. (E.) Pound, A. W. (Dept. Path., U. Queensland, Australia). *Pathology* 2(4): 269-275, 1970.

Initiation of skin tumor formation in white mice by a single short exposure (60 sec) to ultraviolet UV light was studied with UV exposure alone, UV exposure plus painting the skin with a promoting agent (croton oil) after exposure, and with painting the skin with an irritant chemical (croton oil, acetic acid, or xylene) prior to UV exposure. No tumors developed in animals exposed to UV light with no pretreatment or after treatment with irritant chemicals alone; mice pretreated with croton oil, acetic acid, or xylene before UV exposure and painted with croton oil after exposure developed tumors (no. tumors/no. mice; 12/23, 9/20 and 9/16, resp.). Mice exposed to UV light and painted with croton oil after exposure and mice painted with croton oil without UV exposure developed tumors (7/23 and 5/24). Mice pretreated with acetic acid or xylene and then promoted with croton oil without UV exposure also developed tumors (2/21 and 4/28, resp.).

- 0546 CORRELATION OF RADIATION-INDUCED ULTRA-STRUCTURAL CHANGES IN MOUSE HEPATOCYTES WITH ALTERATIONS IN PLASMA CONCENTRATION OF PROTEIN-BOUND NEUTRAL HEXOSES. (E.) Rene, A. A. (Armed

Forces Radiobiol. Res. Inst., Bethesda, Md.) and A. S. Evans. *Radiat Res* 44(1):224-236, 1970.

Liver cell abnormalities induced by whole-body irradiation, and the correlation of these abnormalities with changes in plasma concentration of glycoproteins, were investigated in young adult male mice. Whole body doses of 530 rads of mixed γ -ray-neutron irradiation were administered to rats at rates of 20 rads/min. Although irradiation did not affect the flood concentration of protein-bound carbohydrates (neutral hexoses) in mice which survived the irradiation, concentrations increased from 1.8-2.2-fold in mice which died following irradiation. Electron microscopic examination of the cytoplasmic organelles in hepatocytes of irradiated moribund mice, mice surviving irradiation, and fed and starved unirradiated controls, showed that among the radiation-induced differences were moderate to marked dilatation of the rough endoplasmic reticulum, increased Golgi activity, and rounding of the mitochondria with a decrease in numbers of mitochondrial granules. A correlation between ultrastructural cellular alterations and changed concentrations of protein-bound neutral hexoses was evident.

- 0547 IRRADIATION AS AN ETIOLOGIC FACTOR IN THE DEVELOPMENT OF MELANOMA. (E.) Conley, J. (St. Vincent's Hosp., New York, N.Y.). *Arch Otolaryng* 92(6):627-631, 1970.

Five cases of melanoma involving the lip, cheek and neck, in which radiation therapy appeared to be a causal factor, are described. Patients were of both sexes, and ranged in age from 34-78 yr; radiation therapy had been used for various conditions, including scars, papillomas, and squamous cell cancer of the lower lip. The periods between exposure to therapeutic radiation and onset of melanoma were 40, 6, 5, and 1 yr, and 4 mo. A clear causal relationship between radiation and melanoma was suggested in the cases of short latency, and in cases where melanoma developed at the precise site of radiation treatment. All but 1 of the patients died of their conditions.

- 0548 THE FINE STRUCTURE OF OSTEOSARCOMA PRODUCED EXPERIMENTALLY IN RATS. (E.) Cameron, D. A. (Dept. Path., U. Sydney, Australia). *Pathology* 2(3):223-230, 1970.

White rats received i.p. injections of $1.0 \mu\text{C/g}$ ^{32}P , and thereafter received $0.6 \mu\text{C/g}$ ^{32}P at 2, 4, 6, and 8 wk of age; the fine structure of the osteosarcomata induced by ^{32}P was examined. Twenty tumors were found in the long bones of 16 rats, the period from the last injection to the observation of the first tumor being 32 wk. Most tumors were found in the proximal ends of the tibiae, and in 6 rats metastases were found in the lungs. The fine structure of most of the component cells showed relatively inconspicuous Golgi zones, limited endoplasmic reticulum and few mitochondria; it seemed

PHYSICAL CARCINOGENESIS

unlikely that these cells played much part in matrix synthesis. Other cells more closely resembled osteoblasts, and they were probably derived from the more primitive tumor cells rather than directly from the original bone cells. Presumably they secreted the matrix component of the hard tissue of the tumors. This matrix did not appear to be neoplastic, and its fine structure resembled that of fracture callus. Cells were included within the matrix and were analogous to osteocytes although some of the superficial ones had features of the undifferentiated cells. The few multinucleated cells present resembled osteoblasts, although most of them seemed to be non-functioning and lacked a brush border. Normal endothelial cells lined the thin-walled blood vessels which traversed the tumors.

0549 LONG-TERM RESULTS OF TREATMENT OF THYROTOXICOSIS IN CHILDREN AND ADOLESCENTS WITH RADIOACTIVE IODINE. (E.) Hayes, A. (Harvard Med. Sch., Boston, Mass.), E. M. Chapman and J. D. Crawford. *New Eng J Med* 283(18):949-953, 1970.

The possibility that radioiodine treatment for thyrotoxicosis predisposed patients to cancer either locally in the thyroid or as leukemia was investigated. Thirty patients aged between 8-18 yr were treated with ^{130}I (2 patients) or ^{131}I (28 patients) in doses of from 2-32 mC of ^{131}I for thyrotoxicosis. The average dose/patient was 6.6 mC and the mean length of patient follow-up observation was 9.2 yr. No deaths and no evidence of cancer or leukemia were seen in this series of patients. Prompt remission of the disease was obtained with a single dose in 25 cases. Permanent hypothyroidism developed in 8 patients. Recurrence of thyrotoxicosis associated with benign nodular hyperplasia was observed in 1 case 17 yr after treatment with ^{130}I . Twelve of the females treated with ^{131}I subsequently gave birth to 18 healthy children. One female treated with ^{130}I had an abnormal reproductive history.

See also:

- * (Rev): 0345, 0366, 0370, 0374, 0382
- * (Chem): 0405
- * (Viral): 0578, 0592, 0604, 0605, 0663
- * (Epid-Biom): 0752
- * (Misc): 0770, 0815

VIRAL CARCINOGENESIS

0 COMPARATIVE STUDY OF THE MORPHOLOGY AND DISTRIBUTION OF VIRUS PARTICLES CAUSING LEUKEMIA AND LYMPHOSARCOMA IN MICE, RATS, CATS, AND GUINEA PIGS. (E.) Gross, L. (VA Hosp., Bronx, N.Y.) and D. G. Feldman. *Arch Geschwulstforsch* 1(1):1-9, 1970.

Issues of mice, rats, cats and guinea pigs with leukemia or lymphosarcoma were examined under the electron microscope to compare the morphology and distribution of virus particles in tissues of affected animals. Immature virus particles in leukemic mice were doughnut-shaped with 3 concentric shells and electron-lucent centers; they averaged 100 mμ in diameter and were found in the extracellular spaces and in the cytoplasm of cells. Mature virus particles had nucleoids and were larger than the immature particles, averaging 105 mμ in diameter. Cylindrical and filamentous structures were also found in leukemic mice, usually in the megakaryocytes in the spleen and bone marrow. More particles were found in mice having virally-induced leukemia than in mice with spontaneous leukemia. Virus particles in rat leukemia and lymphosarcoma were structurally similar to those in mice, but rather larger (average diameter, 99 mμ). Spherical virus particles occurred in leukemic cats which were morphologically like the C-type particles found in mice. In cats, particles were found budding from cell membranes; their average diameter was 100-115 mμ.

Leukemic guinea pigs harbored spherical, doughnut-shaped virus particles with electron-lucent centers; particles had nucleoids and were found in perinuclear cisternae in the spleen, lymph nodes, and bone marrow. Guinea pig particles seemed to bud from membranes of the endoplasmic reticulum. Mouse, rat, and cat leukemia virus particles were generally present in larger numbers than in guinea pig virus particles.

1 ENVELOPE ANTIGEN RELATIONSHIPS AMONG THREE HAMSTER-SPECIFIC SARCOMA VIRUSES AND A HAMSTER-SPECIFIC HELPER VIRUS. (E.) Kelloff, G. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), R. Huebner, N. H. Chang, Y. K. Lee and R. V. Gilden. *Int J Cancer* 9(1):19-26, 1970.

Hamster embryo fibroblasts were inoculated with dilutions of one of 3 hamster-specific sarcoma viruses [m-MSV(GLV)(O-H), m-MSV(O-H) or ki-MSV(O-H)] or non-sarcomagenic virus (HaLV), and interference tests were conducted by infecting the resulting cultures with 50-70 focus-forming units of virus; antisera neutralization tests were also performed. The purpose was to determine the immunological relationships among the 4 virus types. The 4 viruses shared at least 1 envelope antigen responsible for neutralization reactions. Specific interference for the sarcoma viruses was obtained in cultures infected with non-sarcomagenic virus. The tested viruses were easily distinguishable from murine C-type viruses in neutralization assays.

2 IMMUNOLOGICAL IDENTITY OF THE GROUP-SPECIFIC ANTIGEN OF HAMSTER-SPECIFIC C-TYPE VIRUSES AND AN INDIGENOUS HAMSTER VIRUS. (E.) Kelloff,

G. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), R. J. Huebner, S. Oroszlan, R. Toni and R. V. Gilden. *J Gen Virol* 9(1):27-33, 1970.

Hamster-specific C-type viruses from chronically infected tissue cultures were used as a source of hamster-specific group specific antigen, which was purified from the infected culture supernatant after being disrupted by ether extraction; the antigen was injected in guinea pigs for the purpose of preparing antisera against it, and the antisera was subjected to immunodiffusion and complement-fixation tests. Reactions of identity were obtained in immunodiffusion tests between all virus preparations while no reactions were obtained with uninfected cells and murine C-type virus preparations. Guinea-pig antiserum to the murine C-type virus group specific antigen did not react with any of the hamster virus preparations. This pattern of specificity was maintained in complement-fixation tests. The hamster-specific sarcoma viruses originally recovered from hamster tumors induced by murine sarcoma viruses, are considered to be pseudotype sarcoma viruses possessing the antigens of the indigenous hamster C-type virus and the sarcoma gene(s) of the original tumor inducing murine viruses.

0553 SYNTHETIC DNA-RNA HYBRIDS AND RNA-RNA DUPLEXES AS TEMPLATES FOR THE POLYMERASES OF THE ONCOGENIC RNA VIRUSES. (E.) Spiegelman, S. (Inst. Cancer Res., Columbia U., New York, N.Y.), A. Burny, M. R. Das, J. Keydar, J. Schlom, M. Travnick and K. Watson. *Nature* 228(5270):430-432, 1970.

Polymerase activity of 6 oncogenic RNA viruses was studied by using synthetic polynucleotides as templates. Analysis of the responses of avian myeloblastosis virus (AMV), feline leukemia virus (FLV), Moloney sarcoma virus (MSV), Rauscher leukemia virus (RLV), mouse mammary tumor virus (MTV), and a rat mammary tumor virus (RMTV) to resident RNA templates, to exogenous DNA (from trypsinized chick embryo cells), and to a synthetic hybrid duplex (dC·rG) indicated that the hybrid directed DNA synthesis ranged from 12 times to 351 times higher than the RNA or DNA directed syntheses. Among the ribohomopolymers, only rC possessed detectable template activity (pmoles nucleotide incorporated/5 min/10 μg viral protein) for AMV-polymerase (3.8), and among deoxyribopolymers, poly dC (11.0), poly dA (1.2), and poly dI (1.2) showed template activity. Except for rC·rG, all the synthetic double-stranded RNA and DNA homopolymers stimulated some incorporation of the complementary nucleotide pairs (the polyribopolymers appeared more effective than the corresponding deoxypolymers except for rC·rG). Some of the synthetic DNA-RNA hybrid duplexes, particularly dC·rG and dI·rC (141.0 and 104.6, resp.), were the most effective templates studied.

0554 NUCLEIC ACIDS-HYBRIDIZATION STUDIES IN NORMAL AND CANCER CELLS. (E.) Valladares, Y. (Natl. Inst. Oncol., City U. Madrid, Spain), Y. Alvarez, E. Tabares and T. Pintado. *Europ J Cancer* 6(9):335-347, 1970.

Hybridization of nucleic acids from normal and cancer cells (agar column technique of Bolton and McCarthy) were investigated. The specificity of DNA-DNA hybridization was demonstrated by the complete complementarity within AV3/INO DNA and salmon-sperm DNA and the complete complementarity within AV3/INO. Complementarity of AV3/INO-human amnion cell DNA and mRNA (with isogenic DNA) reached 89% for DNA-thymidine-³H and 45.5% for mRNA-³²P; after the DNA-mRNA hybridization (44.5%) the DNA still had binding sites for sRNA (9%) and for rRNA (0.6%). Normal mouse embryo DNA with itself showed 90% complementation and cancer virus-induced mouse tumor DNA with itself showed 87% complementation, while mouse embryo DNA confronted with mouse embryo mRNA resulted in 47.2% complementation and confronted with cancer virus-induced mRNA resulted in 37.7% complementation; cancer virus-induced tumor DNA confronted with the virus-induced tumor mRNA or normal embryo mRNA resulted in 46.5% and 31.2% complementation, resp. In the various virus-cell nucleic acids systems studied, part of cancer virus-DNA hybridized with 41,000 parts of cancer virus-induced mouse tumor DNA, 111,000 parts of normal mouse DNA, 399,400 parts of normal hamster DNA, 2340 parts of TC-CV/INO cell DNA, 99,000 parts of TC-SV40/INO cell DNA, or 500,000 parts of normal human amnion DNA.

0555 DNA POLYMERASE ACTIVITY ASSOCIATED WITH RNA TUMOR VIRUSES. (E.) Hatanaka, M. (Flow Lab., Rockville, Md.), R. J. Huebner and R. V. Gilden. *Proc Nat Acad Sci* 67(1):143-147, 1970.

Suspensions of murine leukemia virus, feline sarcoma virus, hamster helper-virus, feline leukemia virus, and viper C-type virus were incubated with a reaction mixture suitable for assay of DNA polymerase activity. Some virus preparations were shaken with ether for 10 min. before incubation. All of the viruses tested stimulated the incorporation of tritiated thymidine triphosphate (³H-TTP) into acid-insoluble material, with the viper virus preparation showing the highest incorporation activity rate (12,825 acid-insoluble cpm); enzyme activity was dependent on the presence of all 4 deoxyribonucleoside triphosphates. Treatment with ether increased DNA polymerase activity with all C-type virus preparations. Ether treatment also prolonged the time of intense DNA polymerase activity, which reached a plateau after 1 hr in untreated preparations and after 2 hr in ether-treated preparations. In ether-treated preparations and untreated preparations, DNA extracted from the reactions sedimented at 2-4S. Some 15-20% of the newly synthesized DNA remained associated with the virions until subjected to SDS-phenol extraction when intact virus was the template, but the DNA synthesized by the ether-treated virus preparations had no firm association with the whole virions and sedimented to the same position in sucrose gradients before and after SDS-phenol extraction.

0556 CELLULAR SURFACE CHANGES INDUCED BY ONCOGENIC VIRUSES AND THEIR ROLE IN MALIGNANT TRANSFORMATION. (Fr.) Montagnier, L. (Fac. Sci. Orsay, France). *Bull Cancer* 57(1):13-22, 1970.

Hamster (BHK 21/13 strain) fibroblasts cultivated on agar nutrient media were used to define stages of Rous or polyoma virus-induced transformation. Cell growth during transformation stage 1a was inhibited by dextran sulfate and promoted by insulin and collagen; cells able to develop without the addition of insulin and collagen and whose growth was less sensitive to dextran sulfate were classified as transformation stage 1b. Transformation stage 2 was characterized by cell growth on agar gel in the presence of dextran sulfate and AMP; lack of growth resulted in inhibition of cell growth by minimal amounts of dextran sulfate in the case of Rous Stage 2b of transformation with polyoma virus. Stage 2 consisted of cell growth capability in the presence of dextran sulfate with no exogenous AMP required. Transition from stage 1 to stage 2 of transformation required increased amounts of exogenous serum. Surface alterations in terms of dye absorbing capacity (ruthenium red) presented thin dye absorbing layers in stage 1a and 1b; these layers were absent in stage 2 and were dependent on the presence of purine nucleotides. Enzyme activity (phosphatase C) in the presence of bivalent ions on specific surface constituents suggested that lecithin phospholipid polar groups of the plasma membrane were being protected by a superficial constituent whose biosynthesis requires exogenous purine nucleotides.

0557 DNA SYNTHESIS BY RNA-CONTAINING TUMOR VIRUSES. (E.) Scolnick, E. M. (National Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), Aaronson and G. J. Todaro. *Proc Nat Acad Sci* 67(1):1034-1041, 1970.

The occurrence of an RNA-dependent DNA polymerase and some characteristics of the polymerase reaction (kinetics, sedimentation, and activity) were studied in oncogenic and non-oncogenic RNA viruses. The *in vitro* DNA polymerase required the 4 essential deoxyribonucleoside triphosphates; the reaction was dependent on temperature (optimal activity at 37°C), and optimal DNA synthesis occurred with Triton X-100 concentration at 0.010-0.03%. Rauscher leukemia virus and Moloney leukemia virus. In a sucrose gradient virion, enzymatic activity and the DNA product that was synthesized cosedimented, suggesting that the 3 are part of a complex. In the DNA polymerase assay, the incorporation (cpm) varied greatly among individual viruses with Rauscher leukemia virus the most active (64,000 compared to its control 430 with only the 4 essential nucleotides in the reaction). Other viruses showing activity were Moloney leukemia virus (5,900 compared to its control 401), Rauscher leukemia virus grown in human cells (2,000 compared to its control 295), Kirsten sarcoma virus (1,050 compared to its control 100), and a mammary tumor virus (1,050 compared to its control 100). The non-oncogenic RNA viruses (Sendai, respiratory syncytial, Newcastle disease, lymphocytic choriomeningitis, and influenza viruses) were inactive.

0558 REVERSION OF VIRUS-TRANSFORMED CELLS TO NORMAL PHENOTYPE ACCOMPANIES RETENTION OF HYPERPLOIDY. (E.) Pollack, R. (New York U. Med. Sch.).

York), S. Wolman and A. Vogel. *Nature* 228(5275): 967-970, 1970.

chromosome number and growth control of virus-transformed mouse cell lines and their revertants were examined. The 4 established cell lines (3T3, 3T6, 3T3, and Py3T3) had similar chromosome modes (73, 74, and 70, resp.) although only 3T3 had growth control. Selected variants (F13T6, F1SV3T3, and Py3T3) exhibited increased chromosome numbers (5, 118, and a bimodal 60, 120, resp.), while the revertants (ReSV3T3 and RePy3T3) had chromosome numbers (72 and 65, resp.) close to those of the transformed parent lines. An increase in chromosome number accompanies reversion, and a decrease accompanies back reversion.

9 SEROLOGICAL STUDIES OF RAT VIRUSES IN RELATION TO TUMORS. (E.) Lum, G. S. (Dept. U. Cincinatti, O.). *Oncology* 24(5):335-343, 1970.

biological differences and differences in infectivity between 2 rat viruses, Kilham and Olivier's virus and the rat virus strain of Lum and Reiner (L-S) were investigated. Inhibition of agglutination in rat sera subjected to heating, potassium periodate and kaolin, the percentage of sera with antibodies against the viruses, and the susceptibility of rats to infection with the viruses were determined. Hemagglutination-inhibition tests in untreated sera of rats infected with the viruses were 5 and 6, resp., for rat virus and L-S virus at a 20-fold dilution of serum. These titers were not affected significantly by heating at 37°C, 56°C, or by potassium periodate treatment. Kaolin treatment, however, reduced the titers of hemagglutinin-inhibitors in all sera tested (titers of less than 1 in both rat virus- and L-S-virus infected sera at a 20-fold serum dilution, resp.). In kaolin-treated sera, serum neutralization titers were even higher than hemagglutination-inhibitor titers. Antibodies against the 2 viruses were found by hemagglutination-inhibition tests in 100% of Long-Evans strain rats, in 58% of Sprague-Dawley rats, in 25% of Wistar rats, and in 0% of Marshall rats. Seventy-eight percent of Wistar rats with either spontaneous adenomata, benign cysts, or X-ray induced tumors had antibodies against 1 or both viruses, whereas none of the sera from rats with transplanted tumors showed virus antibodies. Infectivity tests showed that antibody-free Marshall rats developed fatal infections when injected with rat virus, while L-S virus produced only 42% mortality after a longer elapsed time from injection.

10 CYTOPATHOGENIC AND TRANSFORMATIVE EFFECT OF INFECTIVE AND ONCOGENIC VIRUSES IN TISSUE CULTURE. (Rus.) Zhudina, A. I. (USSR Min. of Health, Leningrad), and O. K. Kuznetzov. *Voprosy* 16(7):47-59, 1970.

cytopathogenic and neoplastic alterations induced by infectious (vesicular stomatitis and smallpox vaccine) and oncogenic (Rous sarcoma) viruses were

compared in chick embryo cell monolayer cultures. Cell disintegration and loss of contact inhibition of motion and reproduction occurred 4 hr after infection with vesicular stomatitis virus, 1 day after smallpox vaccine and 2-12 days after Rous sarcoma virus inoculations, leading to the appearance of morphological transformation foci consisting of epithelioid (in the case of vesicular stomatitis virus) or round basophilic cells with Rous virus. These foci never reached large dimensions and degenerated 5-7 hr after infection with the vesicular stomatitis virus. The smallpox vaccine virus-induced transformation foci (morphologically intermediate between the other two) were larger and more numerous; their degeneration started 24 hr after infection. The Rous virus-induced foci were the largest and the most numerous and never degenerated. An increase in cell basophilia, an enlargement of cell nucleoli and the development of symplastic areas (this latter was more manifested in case of the smallpox vaccine virus) were a common response to all 3 viruses. Intensified mitotic activity with temporary (24 hr) cell proliferation occurred in the smallpox vaccine virus-induced transformation foci; such proliferation was unlimited in the case of Rous virus-induced transformation. The proliferation stage is most likely a forerunner of malignancy. Oncogenicity of the smallpox vaccine virus in newborn mice is reviewed.

0561 STUDIES ON FBJ VIRUS-INDUCED BONE TUMORS IN MICE. (E.) Yumoto, T. (U. Texas M.D. Anderson Hosp. Tumor Inst., Houston), W. E. Poel, T. Kodama and L. Dmochowski. *Texas Rep Biol Med* 28(1-2):145-165, 1970.

Newborn mice of strains ICR and BALB/c received i.p. injections of 0.1 ml dilute virus-induced bone tumor extract, and 8-wk-old GP strain mice were implanted s.c. with bone tumor mince induced in GP mice by tumor extract, to investigate histologically the tumorigenic activity of bone tumor-inducing virus in animals. Bone tumors of the spine, ribs and/or long bones developed in 7 of 12 GP mice; and 3 developed bone tumors. None of the BALB/c or ICR mice developed bone tumors. Transplantation of the induced bone tumors from GP mice was successful in other mice of the same origin. Comparative light and electron microscope studies carried out on the induced and transplanted bone tumors in GP and CF1 mice showed that the tumors induced in GP and CF1 mice, with few exceptions, were periosteal osteosarcomas and paraosteal tumors containing calcified and uncalcified osteoid and chondroid. Osteogenic, chondrogenic, fibrosarcomatous and undifferentiated round or spindle cell areas of proliferation were frequently observed in the same tumor, but osteolytic tumors were not seen. Budding, immature and mature type C virus particles were seen in all tumors as well as in non-tumorous organs of the tumor-bearing mice. Type C virus particles and budding from plasma membrane were seen in large numbers in long-term tissue cultures derived from the induced tumors of CF1 and GP mice. Close similarity in both

structure and virus particle content of the induced and transplanted tumors in CF1 and GP mice was found. A neoplastic response of multipotential mesenchymal cells to viral infection seems to be implicated in bone tumors induced in the present study.

- 0562 GROUP-SPECIFIC ANTIGEN EXPRESSION DURING EMBRYOGENESIS OF THE GENOME OF THE C-TYPE RNA TUMOR VIRUS: IMPLICATIONS FOR ONTOGENESIS AND ONCOGENESIS. (E.) Huebner, R. J. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) G. J. Kelloff, P. S. Sarma, W. T. Lane, H. C. Turner, R. V. Gilden, S. Oroszlan, H. Meier, D. D. Myers and R. L. Peters. *Proc Nat Acad Sci* 67(1):366-376, 1970.

Mouse embryos under 12-14 days in term were tested for the presence of a group-specific antigen of the C-type RNA tumor virus; embryos of all strains tested revealed detectable titers of group-specific antigen in the liver, spleen or thymus. Younger, rather than older, embryos were likely to be antigen-positive, particularly in those strains which normally revealed little or no expression of the RNA genome postnatally. The antigens were found in embryos of low-leukemia strains, free of infectious virus. The genome of RNA tumor viruses without infectious virus expression may be vertically transmitted as part of the natural genetic apparatus of normal mouse cells. Since group-specific antigens have also been described in chick embryos and immunological tolerance to homologous group-specific antigens has been demonstrated in hamsters and cats as well as in mice and chickens, the hypothesis has been extended to include vertebrate cells in general. The high incidence and titers of the group-specific antigen suggest that the genes for RNA tumor virus may be important as gene determinants in the developing embryo, in addition to acting as determinants of carcinogenesis.

- 0563 MORPHOLOGICAL VARIATION OF A SYNCYTIAL VIRUS FROM LYMPHOSARCOMATOUS AND APPARENTLY NORMAL CATTLE. (E.) Boothe, A. D. (Natl. Anim. Dis. Lab., Ames, Iowa), M. J. Van Der Maaten and W. A. Malmquist. *Arch Ges Virusforsch* 31(3-4):373-384, 1970.

Bovine embryonic spleen cell cultures were infected with bovine syncytial virus which had been isolated from both normal cattle and cattle bearing lymphosarcomas, and infected cells were examined by electron microscopy. A double-membrane enveloped virus particle associated with the endoplasmic reticulum were found in the cytoplasm of the cells. These particles consisted of nucleocapsids measuring 35-45 mμ in diameter; 2 or more nucleocapsids were sometimes contained in the same membrane envelope. The endoplasmic-reticulum-associated viral particle had a nucleocapsid morphologically similar to that of bovine syncytial virus, and it was associated with bovine syncytial virus immunofluorescence. It occurred in the same cells and cell cultures as bovine syncytial virus, and it could not be demonstrated in cell cultures in the absence of bovine syncytial virus. On the basis of the 4 latter findings, it appears that the double membrane

enveloped, endoplasmic reticulum-associated viral particles observed were an aberrant form of bovine syncytial virus.

- 0564 INFLUENZA VIRUS AND LUNG CARCINOMA IN EXPERIMENTS. (Ger.) Staemmler, M. (Rechenberg Lab. Chem., Grunenthal GmbH., Stolberg, Germany), Foitzik and M. Heydenrich. *Z Krebsforsch* 74(3):283-294, 1970.

The effect of intranasal administration of influenza virus A, strain PR 8 in dilutions of 10^4 - 10^6 , in C57BL/6 mice was investigated. The first experimental group was infected with the virus under light ether anesthesia using a 0.1 ml suspension. The animals were dissected immediately after death and a suspension of lung tissue (with the adapted virus) was prepared for injection into another group of mice. Of the 323 animals infected, 136 died within the first 6 days; a second group of 248 mice received the virus administration without prior adaptation. Of the 571 animals thus treated, 248 survived the first 6 days, but most of the animals died within 20 days of the infection. Histological examination suggested the appearance of early changes in the alveoli predominantly of the squamous type, with the later ones showing the adenocarcinoma type cells.

- 0565 TRANSMISSION OF AN AMPHIBIAN LYMPHOSARCOMA TO AND THROUGH INSECTS. (E.) Nayar, K. K. (Dept. Zool., U. Kerala, Trivandrum, India), E. Arthur and M. Balls. *Oncology* 24(3):377, 1970.

Toads (*Xenopus laevis laevis*) were given implants of living or frozen lymphosarcoma, and extracted from the induced lymphosarcomas from spleen, liver, and kidney of the toads were implanted in cockroaches. The salivary glands of all of the toads which survived (163/174) were affected by aggregates of hemocytes. Fractions of the abnormal roach tissue which were then transferred to young mature *Xenopus* caused the development of lymphosarcomas in the toads in 30/57 cases. Infectivity appears to have been retained during passage through the insects, suggesting that insects can be used as reservoirs of infectivity for vertebrate lymphosarcomas.

- 0566 EVIDENCE FOR A DNA REPLICATIVE GENOME IN RNA-CONTAINING TUMOR VIRUSES. (E.) J. P. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and A. V. Bader. *Proc Nat Acad Sci* 67(2):843-850, 1970.

The requirement for DNA synthesis in the replication of RNA tumor viruses (Rous sarcoma virus, avian leukosis virus) immediately after infection was studied in chick embryo cells using 5-bromodeoxyuridine (BrdU). Treatment of the cells with BrdU (100 μg/ml) immediately following exposure to virus resulted in a significant decrease in the number of infectious virus although general cellular pro-

RNA or RNA synthesis, mitosis, and cell growth) showed no differences from controls during the first 2 days after BrdU treatment. The physical numbers of virions (electron microscopy) were similar in BrdU-treated and untreated cultures, and no morphological differences were observed. Cell transformation was not affected by BrdU and virus-specific antigen appeared at approximately the same time (24 hr after infection) and in the same amounts (1:32 complement fixation titers⁻¹). The replicative genome of RNA-containing tumor viruses apparently contain DNA.

7 TRANSMISSION OF MOUSE NEUROBLASTOMA BY A CELL-FREE EXTRACT. (E.) Prasad, K. N. (Colorado Med. Ctr., Denver), J. Zambarnard, R. Her and M. H. VanWoert. *Nature* 228(5275): 997-1000, 1970.

Tyrosine hydroxylase enzyme activity and tumor induction by a cell-free extract (CFE) of neural tumors which originally developed in C1300 mice were investigated. CFE was prepared from putative neuroblastomas induced in mice by inoculation with tumor tissue from the original strain, and injected into mice in amounts of 0.4 ml per test mice; the tumorigenic efficacy of CFE was compared to that of tumor-transplanted neoplasms. CFE-injected mice developed palpable tumors in 18-40 days from time of injection, while mice which were given tumor transplants developed tumors in 8-10 days. All treated mice developed tissue-induced tumors, while 75% of CFE-injected mice developed tumors. Most tumors developed at the injection site (right axillary region); but the neck and intraperitoneal cavity were also affected. CFE-induced tumors were transplantable with the same efficiency as the tissue-transplantation-induced tumors. Tyrosine hydroxylase was found in similar amounts (30.5 nmoles/hr/g protein) in CFE-induced and transplantation-induced tumors, indicating that the CFE transmitted the same tumor as that which was transplanted.

8 ENZYMIC BLOCK IN THE SYNTHESIS OF GANGLIOSIDES IN DNA VIRUS-TRANSFORMED TUMORIGENIC MOUSE CELL LINES. (E.) Cumar, F. A. (Nat'l. Inst. Neurol. Dis. Stroke, Nat'l. Inst. Hlth., Bethesda, Md.), R. O. Brady, E. H. Kolodny, V. W. Parland and P. T. Mora. *Proc Nat Acad Sci* 67(2): 764-766, 1970.

Ganglioside synthesis was investigated in tumorigenic virally-transformed mouse cells to determine the reason for the decrease of gangliosides with an oligosaccharide chain larger than sialyllactose in virally transformed cells compared to parent cells or spontaneously-transforming cells. Mouse cell lines transformed by SV40 and polyoma virus were employed. Catabolism of gangliosides by enzymatic hydrolysis of sialic acid-labeled gangliosides was significantly increased in virally transformed cells, indicating that the decrease of gangliosides was not due to excessive catabolism. However, the enzyme catalyzing the transfer of *N*-acetylneuraminyl-

galactosylglucosyl ceramide was drastically reduced in virally transformed cells. These findings appear to indicate that the decrease of gangliosides in virally transformed cells is due to impaired synthesis of tri- and tetrahexosyl gangliosides in these cells, the impairment being due specifically to a block in a required step for the biosynthesis of these ganglioside homologs.

0569 ELECTRON MICROSCOPIC STUDY OF VIRUS-LIKE PARTICLES IN HUMAN LEUKEMIA AND ALLIED DISEASE. (E.) Yumoto, T. (Fac. Med. Kyushu U., Fukuoka, Japan). *Acta Haemat Jap* 32(4):578-592, 1970.

Biopsy material and plasma pellets from patients with leukemia and lymphoma conditions were studied under the electron microscope to detect virus particles in human leukemia and related conditions. Type C virus particles resembling those associated with murine leukemia were found in plasma pellets prepared from 7 of 13 leukemia or lymphoma patients. These particles were generally spherical, averaging 1800 Å in diameter; some exhibited a tail-like structure. Biological activity of these virus-like particles has not yet been demonstrated. The examination of ultra-thin sections of leukemic tissues revealed only occasional virus particles, very few in number. A virus-like particle resembling budding at the plasma membrane was observed in a biopsied lymph node specimen from a patient with Hodgkin's disease. Occasionally intracisternal and intracytoplasmic type A virus particles were also seen in leukemic cells and reticuloendothelial cells; intracytoplasmic type A particles were present only in the cytoplasm of plasma cells.

0570 VIROLOGICAL STUDIES ON HUMAN LEUKEMIA AND ALLIED DISEASES. (E.) Ito, Y. (Aichi Cancer Ctr., Nagoya, Japan). *Acta Haemat Jap* 32(4):569-577, 1970.

The possibility of a viral etiology for leukemia and allied diseases was examined in transformed "whole" human embryonic (THE) cell lines established from human embryonic cells and the cell-free supernatant of leukemic cell cultures. Three cell lines (THE-1, -2, and -3) were established, but the THE-1 (derived from an epithelioid focus) became contaminated and was abandoned, while the remaining 2 cell lines (derived from round cell foci) grew in floating clumps, exhibited typical herpes-type or Epstein-Barr virus (EB) particles and lesions in #10 chromosome (the extra chromosome in the occasionally observed trisomy of the #10 chromosome also exhibited this lesion). Attempts to establish a transformed cell line from the lymphatic tissues of patients with Hodgkin's disease have not been successful. A carrier hypothesis in which lymphoblastoid cells presumably host the EB virus either in a repressed (dormant) or functioning state has been proposed (transfer of the EB virus genome from the carrier cell to a recipient may initiate the

neoplastic process by the action of or the interaction with the transferred virus genome).

- 0571 THE INCIDENCE OF "LEUKOVIRUS" IN CULTURED HUMAN HEMATOPOIETIC CELLS. (E.) Moore, G. E. (Roswell Park Mem. Inst., Buffalo, N. Y.), H. Kitamura and J. Minowada. *J Surg Oncol* 2(4): 385-392, 1970.

Despite the difficulty of detection by electron microscopy, a herpes-like virus has been found in almost 30% of hematopoietic cell lines established from patients with leukemia, lymphoma, melanoma, and other malignancies and in approximately 70% of the cell lines derived from healthy individuals. The virus may destroy some cells in the affected cell line, but preliminary efforts to infect established non-virus-containing cell lines with the virus resulted in only 1 out of 5 takes.

- 0572 SELF-REPLICATING RNA IN LEUKEMIC CELLS. (E.) Watanabe, I. (Sch. Med. Keio U., Tokyo, Japan) and I. Haruna. *Acta Haemat Jap* 32(4):593-602, 1970.

Self-replicating RNA (viral RNA or genetic RNA) was detected in mouse and human leukemic cells by measuring RNA template activity (^3H -uridine triphosphate incorporation into the acid-insoluble fraction) on the specific RNA-dependent RNA polymerase (RNA replicase). Poliovirus-infected HeLa cells, echovirus-infected FL cells, and Friend virus leukemic cells of mice contained self-replicating RNAs. Ehrlich ascites tumor cells and human acute myeloid leukemic cells were found to contain RNA-dependent RNA polymerase and its template RNA. An ethine derivative (M1124), which is a specific inhibitor for RNA replicase of Q β phage, inhibited specifically the RNA-dependent RNA polymerase from tissues of mice with Friend disease, poliovirus-infected HeLa cells, and myeloblasts of human acute myeloid leukemia, suggesting that these polymerases are RNA replicases.

- 0573 EXCRETION OF IMMUNOGLOBULINS IN BURKITT'S LYMPHOMA. (E.) McFarlane, H. (Dept. Chem. Path., U. Ibadan, Nigeria), R. O. Barrow, V. A. Ngu and B. O. Osunkova. *Brit J Cancer* 24(2):258-265, 1970.

Urine and blood samples were collected from 17 patients with Burkitt's lymphoma, in order to identify and quantitate the immunoglobulins in their urine and sera. Gel filtration revealed IgM in the urine of 4 of the 17 patients, and in none of the control subjects. This IgM emerged from Sephadex G200 column in 2 different peaks strongly suggesting subunits of the intact molecule. The total protein excreted in the urine of Burkitt's lymphoma patients is higher than in controls (127 mg vs 90 mg) for controls, and may be due to renal involvement. Intact IgA and IgG as well as fragments of IgG were present in the urine of all Burkitt patients as well as in controls. Twelve of 16 Burkitt's lymphoma patients had reduced serum IgM (0.57 vs 1.23

mg/ml for controls), and 6 of these had reduced serum IgG.

- 0574 EBV DNA IN BIOPSIES OF BURKITT TUMOR ANAPLASTIC CARCINOMAS OF THE NASOPHARYNX. (E.) Zur Hausen, H. (Inst. Virol. U. Wurzburg, Germany), H. Schulte-Holthausen, G. Klein, W. Henle, P. Clifford and L. Santesson. *Nature* (5276):1056-1058, 1970.

Epstein Barr (EB) viral DNA in tumor cells of Burkitt's lymphoma and nasopharyngeal carcinoma were detected and quantitated by the nucleic acid hybridization technique. Cellular DNA annealed with increasing amounts of EBV ^3H -DNA permitting calculation of viral genome equivalents/cell. Burkitt tumor cells contained 2-26 genome equivalents and nasopharyngeal carcinomas contained 1-19 genome equivalents, while other tumors tested (Marek's disease, Hodgkin's disease, squamous cell carcinoma) and human KB cells, Nil-2 cells of hamster origin, cytomegalovirus-infected Wi-38 cells failed to anneal. Positive controls (an EBV carrier cell line D 75) hybridized with 17% of the input EBV ^3H -genome equivalents/cell. Studies of cellular DNA with herpes simplex virus (HSV) ^3H -DNA indicated that the positive control (DNA from HSV-infected Nil-2 cells) annealed with 17% of the input ^3H -DNA while the D 75 cells failed to anneal. Nucleic acid is regularly detected in biopsies of Burkitt's lymphomas and anaplastic carcinoma of the nasopharynx.

- 0575 VIRAL ETIOLOGY OF HUMAN MALIGNANT LYMPHOMAS. (E.) Oboshi, S. (Nat'l Cancer Ctr. Res. Inst., Tokyo, Japan). *Acta Haemat Jap* 32(4):619, 1970.

The relation of Burkitt's tumor and childhood lymphomas was discussed, and 5 continuous suspension cultures that were derived from human lymph nodes were characterized. The starry-sky appearance of Burkitt's tumor (macrophages interspersed among tumor cells) was frequently observed in children's cases of conventional lymphosarcoma and reticulum cell sarcoma but rarely seen in adult cases (suggesting a relation to childhood lymphomas in general). The characteristic primitive appearance, uniform size and maturity of Burkitt's tumor cells were also detected in 2 cases of poorly differentiated lymphosarcoma. Leukemic transformation rarely occurred in Burkitt's tumor, but once it did the disease could not be distinguished from lymphatic leukemia, indicating that these diseases may be different manifestations of the same entity. Of the 5 cell lines established, RS-2, RS-3, IM-1 contained normal lymphoreticular cells; MC-12 contained both neoplastic and normal lymphoreticular cells. The cells of RS-3 and MC-12 reacted with antibody to only 1 class of immunoglobulins (anti-IgA and anti-IgG, resp.), and RS-2 reacted with anti-IgG and anti-IgM, while RS-3 and MC-12 reacted with all 3 classes (anti-IgG, anti-IgM, and anti-IgA). The Epstein-Barr virus was detected in all 5 cell lines indirectly by immunofluorescence and in the RS-2 and MC-12 lines

tly by electron microscopy (the larger amounts of these cell lines may explain the detection in these cell lines).

6 SO-CALLED C-MARKER CHROMOSOME AND EPSTEIN-BARR VIRUS. (E.) Whang-Peng, J. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), P. Ober and T. Knutsen. *J Nat Cancer Inst* 45(4): 839, 1970.

For human cell lines, 2 infected with Epstein-Barr virus and 2 already containing the virus, were subjected to cytogenetic studies to detect the presence of the "C marker" chromosome, a chromosome having a distinctive secondary constriction or chromosome gap in the long arm of 1 or both chromosome pairs; the aim was to test the specificity of marker chromosome as an indicator of present or past infection with Epstein-Barr virus. In each cell the incidence of gaps and secondary constrictions increased as the total number of chromosomal aberrations increased. Only 1-2% of the cells in lines with 20-90% Epstein-Barr virus-infected cells had the C marker chromosome, and there was no evidence that this abnormality was related to Epstein-Barr virus. Apparently, the C marker chromosome is a random gap caused perhaps by a nonspecific viral infection and not a true secondary constriction.

7 INFECTIOUS MONONUCLEOSIS: SERUM ANTIBODIES AGAINST THE EPSTEIN-BARR-VIRUS. (E.) Gsell, H. O. (Inst. Microbiol. Hyg., U. Basel, Switzerland) and B. Müller. *Klin Wschr* 19(19):1107-1110, 1970.

The presence of Epstein-Barr virus (EBV) serum antibodies and heterophilic infectious mononucleosis (IM) antibodies was investigated in 13 IM patients; they were examined within 28 days of the onset of illness and 7-96 days later. Two of these patients had heterophilic IM antibodies had no EBV antibodies; another patient had first a positive and later a negative EBV antibody test, and one patient exhibited a positive EBV test 68 days after the onset of IM, following a recurrence of IM. It was concluded that approximately 10-15% of the IM patients have no EBV antibodies and that possibly IM could not be attributed to a single etiological factor. The role of the EBV as the main etiological factor of IM is still open.

8 INCREASE IN ANTIBODY TITER AGAINST THE EBV-ASSOCIATED MEMBRANE ANTIGEN COMPLEX IN BURKITT'S LYMPHOMA AND NASOPHARYNGEAL CARCINOMA AFTER LOCAL IRRADIATION. (E.) Einhorn, N. (Karolinska Hosp., Stockholm, Sweden), G. Klein and P. Lifford. *Cancer* 26(5):1013-1021, 1970.

The effect of local irradiation (200-6500 r) on the titer of the antibody against the Epstein Barr virus-associated membrane antigen complex in Burkitt's lymphoma and nasopharyngeal carcinoma was studied by titrating the blocking activity of antibodies in the serum against a fluorescein isocyanate-conjugated reference immunoglobulin (F-

Mutua) derived from a case of Burkitt's lymphoma in long term remission. The sera from patients were tested before, at the termination of, and 6-9 weeks after local irradiation of the tumor with Burkitt's lymphoma-derived lymphoblastoid cell lines as target cells. Significant increases in the titer of membrane-reactive antibodies were observed at several serial dilution levels in sera of 2 patients with Burkitt's lymphoma and 3 patients with nasopharyngeal carcinoma but not in the sera of control patients (Hodgkin's disease, laryngeal carcinoma, and lymphosarcoma).

0579 SURFACE ANTIGENS ON LYMPHOBLASTOID CELLS DERIVED FROM NASOPHARYNGEAL CARCINOMA. (E.) De Schryver, A. (Karolinska Inst. Stockholm, Sweden), G. Klein and G. De The. *Clin Exp Immun* 7(2):161-171, 1970.

The Epstein-Barr virus-associated surface antigens of Burkitt's lymphoma and infectious mononucleosis derived lymphoblastoid cell lines were compared with the corresponding surface antigens of a lymphoblastoid cell line from a case of nasopharyngeal carcinoma for their reactivity with Epstein-Barr virus positive reference conjugates and for their blocking reactions with sera derived against the conjugates. The reactivity of the nasopharyngeal carcinoma cells correlated well with the Burkitt's lymphoma and infectious mononucleosis type cells in blocking tests with reference conjugates (r of 0.90 with Mutua-conjugate and r of 0.66 with Kipkoeh-conjugate) and r of 0.60 with unconjugated sera. The results do not support the existence of membrane expressed antigenic differences between nasopharyngeal carcinoma and Burkitt's lymphoma or infectious mononucleosis derived cell lines, although differences may exist which were not detected with these methods.

0580 SINGULARITY OF ONCOGENIC ACTIVITY OF STRAIN MC29 AVIAN LEUKOSIS VIRUSES. (E.) Beard, D. (Duke U. Med. Ctr., Durham, N. C.), J. F. Chabot, A. J. Langlois, E. A. Hillman and J. W. Beard. *Arch Geschwulstforsch* 35(4):315-325, 1970.

White leghorn chicks, 1-15 days old, were given i.p. or i.v. inoculations of avian tumor virus, strain MC29, obtained from diseased chicks or from tissue culture in order to investigate the host's oncogenic response to strain MC29 virus. Chicken response to strain MC29 virus was characterized by the formation of neoplasms derived chiefly from myeloid hematopoietic tissue, including myelocytoma, anaplastic sarcoma, and myelocytomatosis. Erythroid and lymphoid tumors were also observed. Kidney tumors included cystadenoma, and liver tumors included rifted adenoma and carcinoma. Tumors of the peritoneum, epicardium and pericardium included mesothelioma and chondroma. The liver was the preferred site for various growths varying from many nodules to general enlargement due to myelocyte infiltration. MC29 virus infection was generally not leukemogenic. MC29 responses which are unique to neoplasms caused by other leukosis or

avian tumor viruses include primary liver growth and the induction of mesotheliomas in the peritoneum or pericardium. Another singular activity of MC29 is rapid infection and massive alteration of chick embryo cells. These findings suggest an etiologic individuality for strain MC29 compared to other viral strains causing erythroblastosis or myeloblastosis.

- 0581 THE INFLUENCE OF ULTRAVIOLET-INACTIVATED SENDAI VIRUS ON MAREK'S DISEASE VIRUS INFECTION IN TISSUE CULTURE. (E.) Hlozanek, I. (Czechoslovak Acad. Sci., Prague). *J Gen Virol* 9(1):45-50, 1970.

Mixtures of Marek's disease virus (containing 23,000-46,000 plaque-forming units) and chick kidney cells were exposed to UV-inactivated Sendai virus (1000-4000 hemagglutination units) in an attempt to determine whether the inactivated Sendai virus affected the transfer of Marek's disease virus from infected to uninfected cells. The presence of UV-inactivated Sendai virus increased the transfer of Marek's disease virus from infected to uninfected chick kidney cells by as much as 50-100%. This effect was seen after incubation of infected and uninfected chick kidney cells in the presence of UV-inactivated Sendai virus at 4°; only a slight further increase in transfer of infection with subsequent incubation at 37° was seen. The close apposition of infected and uninfected cells occurring during the agglutination produced by treatment with UV-inactivated Sendai virus in the cold, rather than complete cell fusion may have been the main means by which the transfer of infection was increased by treatment with UV-inactivated Sendai virus. However, phytohemagglutinin stimulated agglutination was ineffective in transferring the infection, which indicates that this effect is specific for Sendai virus.

- 0582 ISOLATION OF A SECOND AVIAN LEUKOSIS GROUP-SPECIFIC ANTIGEN 9gs-b) FROM AVIAN MYELOBLASTOSIS VIRUS. (E.) Allen, D. W. (Massachusetts Gen. Hosp., Boston,), P. S. Sarma, H. D. Niall and R. Sauer. *Proc Nat Acad Sci* 67(2): 837-842, 1970.

The isolation of a group-specific antigen (Gs-b) from avian myeloblastosis virus is described. Avian leukosis virus from peripheral blood of leukemic chicks was treated with Tween 80 and ether, and subjected to column chromatography and carboxymethyl-cellulose chromatography. Immunological examination of the isolated antigen was conducted by gel electrophoresis, complement-fixation tests, and N- and C-terminal amino acid analysis. Chromatographic analyses of the antigen constituents of the viral protein showed that antigen gs-a was eluted at pH 5.2, whereas the known antigen gs-b was eluted at pH 6.1. The molecular wt of gs-a was about 20,000, while that of gs-b was 11,000. Complement fixation titers of the antigens at concentrations of 0.5 mg/ml were 512 for gs-a and 64 for gs-b, using anti-gs-a rabbit serum as antiserum. Leucine was the only N-terminal amino acid evident after reaction of gs-b

with ¹⁴C-dinitrofluorobenzene, while proline was the N-terminal residue of gs-a.

- 0583 STUDIES ON SINGLE FOCI OF HEMATOPOIETIC TRANSFORMED BY AVIAN MYELOBLASTOSIS VIRUS. (E.) Moscovici, C. (VA Hosp., Gainesville, FL) and M. Zanetti. *Virology* 42(1):61-67, 1970.

The cultivation of myeloblasts from single foci obtained after avian myeloblastosis virus (AMV) infection of 3 different genetic types of chick embryo yolk sac cultures is described. AMV dilutions of 10¹ yielded an average of 200 transformation foci/culture dish, and the virus dilution 10³ yielded 2 foci at most. Transformed foci were transferred to feeder cultures of Japanese quail fibroblasts, and supernatant fluids from culture foci were subjected to fluorescence and interference tests and were injected into embryonated chicken eggs to test for the presence of infectious virus; foci were found to contain viruses of group A or B. Several foci were found to be free; these nonproducer myeloblasts were infected with 4 different nontransforming avian leukosis viruses, including Rous-associated virus 7 and 2 strains of myeloblastosis-associated virus in an attempt to recover avian myeloblastosis from the nonproducing cells. Avian myeloblastosis virus could be recovered only when either strain of Rous-associated virus was added to nonproducing cultures.

- 0584 MECHANISM OF CARCINOGENESIS BY RNA VIRUSES: III. FORMATION OF RNA-DNA COMPLEX AND DUPLEX DNA MOLECULES BY THE DNA POLYMERASE(S) OF AVIAN MYELOBLASTOSIS VIRUS. (E.) F. K. (Aichi Cancer Ctr., Nagoya, Japan), J. T. J. W. Beard, D. Beard and M. Green. *Proc Nat Acad Sci* 67(3):1432-1439, 1970.

Steps in DNA synthesis by DNA polymerase of avian myeloblastosis virus (AMV) were investigated. DNA was prepared from the plasma of diseased birds. DNA polymerase activity was exposed by treatment with the nonionic detergent Nonidet P-40 (0.05%). DNA polymerase in the virus displayed a rapid synthesis of viral DNA, consisting of the formation of an RNA-DNA hybrid molecule, and duplex DNA molecules. The kinetics of deoxythymidine triphosphate incorporation into DNA were biphasic: an initial rapid reaction for 4 min at 37°C with a minimum polymerization rate of 10-20 nucleotides/sec, and a second reaction at about half the initial rate. RNA-DNA complexes were detected as early as 3 min after the initiation of DNA synthesis; DNA from template was formed after 7, 20 and 60 min of reaction. Most of the free AMV DNA formed an RNA-DNA hybrid when annealed with viral RNA. Over half the free AMV DNA product was apparently double-stranded, since it was retained on hydroxyapatite after elution with 0.12 M phosphate buffer, and was resistant to *Escherichia coli* exonuclease I. The virus or calf-thymus DNA added to unmasked AMV DNA synthesis 4-16-fold if there was no competition with RNase, and 40-130-fold if RNase treatment

ceeded the enzyme assay. A single enzyme may form the RNA-DNA hybrid and the duplex DNA product; alternatively, 2 polymerases may be present in the reaction.

55 ISOLATION OF AMINO ACID ACCEPTOR RNA FROM PURIFIED AVIAN MYELOBLASTOSIS VIRUS. (E.) Erikson, E. (U. Colorado Med. Ctr., Denver, Colo.) and R. L. Erikson. *J Molec Biol* 52(2):387-390, 1970.

The aminoacylation capacity for various amino acids was tested in the fractional RNA component of the avian myeloblastosis virus which had previously been found to have a sedimentation coefficient of 18S, and to comprise 40% of isolated viral RNA. This fractional RNA was aminoacylated by aminoacyl-transfer RNA synthetases prepared from homogenates of chick embryos. Chick embryo RNA and the myeloblast RNA had nearly equal aminoacylation capacities for amino acids tested. Viral transfer RNA had acceptor activity for the amino acids valine, proline, glycine, methionine, asparagine and arginine at levels equal to or approaching that of an equal amount of transfer RNA from chick embryo or from the source of the RNA myeloblasts. Aminoacylation figures for avian myeloblastosis virus RNA and chick embryo RNA for various amino acids showed that viral RNA accepted 27.6 μ moles of valine/ μ g RNA, while chick embryo RNA accepted 19.0 μ moles of valine/ μ g RNA, while chick embryo RNA accepted 19.0 μ moles valine/ μ g RNA. Viral RNA and chick embryo accepted 3.9 and 5.9 μ moles proline/ μ g RNA, resp. The amino acids tyrosine, isoleucine, phenylalanine, threonine, and arginine were accepted in negligible amounts by the viral RNA. Apparently, host cells and the 4S RNA found in avian myeloblastosis virus do not have the same amino acid-accepting activity.

56 VIRAL DNA-DEPENDENT DNA POLYMERASE AND THE PROPERTIES OF THYMIDINE LABELED MATERIAL IN VIRIONS OF AN ONCOGENIC RNA VIRUS. (E.) Riman, J. (Inst. Organic Chem., Biochem., Czechoslovak Acad. Sci., Prague) and G. S. Beaudreau. *Nature* 228(270):427-430, 1970.

DNA-dependent DNA polymerase activity and a thymidine labeled material that were found in the virions of avian myeloblastosis (AMV) were studied by buoyant density gradients. Polymerase activity measured by the incorporation of 3 H-deoxythymidine triphosphate into acid insoluble material) was stimulated by DNA templates (intact or denatured) from birds and mammalian cells, but the enzyme activity (pmoles incorporated) with denatured bacterial (*Streptomyces chrysomalus*) DNA (rich in guanine and cytidine) was 15 times higher (15.10) than with the avian (0.97) or mammalian (1.00) DNA and 70 times higher than the endogenous (0.22) activity. The AMV enzyme lost activity when one of the 3 deoxynucleoside triphosphates (dATP, dGTP, or dTTP) was omitted from the incubation mixture indicating that a heteropolymer is the product of synthesis. Analysis of the phenol extract from a

reaction mixture with the polymerase and template DNA (*Streptomyces chrysomalus*) on a cesium chloride gradient indicated that the DNA copy corresponded to its template. 3 H-Thymidine labeled material isolated from AMV and banded on cesium chloride gradients showed a large fraction of the DNA rich in the guanine and cytidine content and a minor component rich in adenine and thymine.

0587 COILED STRUCTURE OF THE NUCLEOCAPSID OF AVIAN MYELOBLASTOSIS VIRUS. (E.) Lacour, F. (Inst. Gustav Roussy, Villejuif, France), A. Fourcade, C. Verger and E. Delain. *J Gen Virol* 9(1):89-92, 1970.

A method for the disruption of avian myeloblastosis virus and isolation of the nucleocapsid components is described. Pellets of avian myeloblastosis virus, partially purified from leukemic chicken plasma by differential centrifugation, were suspended in distilled water containing a final concentration of 0.05% (w/v) of deoxycholate and 0.05% (w/v) of Brij 58, freshly dissolved. Electron microscopic examination of the centrifuged suspension showed that the pooled material consisted of nucleocapsids. The nucleoids had an internal granular, organized structure consisting of an annular form, a loose coil or volute, and an unrolled form with a diameter of 30-70 nm and a length of 0.5-1 μ m. The possibility that the structures observed were derived from mycoplasma was excluded by the absence of mycoplasma in both aerobic and anaerobic plasma cultures.

0588 ULTRASTRUCTURAL STUDIES OF FELINE LEUKEMIA VIRUS. (E.) Dougherty, E., III (New York St. Vetr. Coll., Ithaca) and C. G. Rickard. *J Ultrastruct Res* 32(5-6):472-476, 1970.

Seven spontaneous and 5 experimentally-induced cases of feline lymphosarcoma were examined by electron microscopy for feline leukemia virus; tissues searched for virus included adrenal glands, bone marrow, liver, lung, pancreas and ovary. C-type viral particles were found in 11 of 12 bone-marrow samples, in 6/12 lymph nodes, in 5/15 thymuses, in 3/12 intestines, in 3/12 livers, in 3/12 spleens, and in 2/12 lungs. Envelope spikes and intermediate membranes of viral particles were found in 11/12 and 4/12 of cat lymphosarcomas, resp. The envelope spikes consisted of 2 bars, parallel, crossed or V shaped; they measured 70-150 Å in length; intermediate membranes were found equidistant between the bimolecular envelope and the nucleoid. The shape and number of envelope spikes was seemingly uniform enough to suggest that they may be normal structural parts of the viral particle.

0589 SEPARATION OF RNA-DEPENDENT DNA POLYMERASE ACTIVITY FROM THE MURINE LEUKEMIA VIRION. (E.) Gerwin, B. I. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), G. J. Todaro, V. Zeve, E. M. Scolnick and S. A. Aaronson. *Nature* 228(5270):435-438, 1970.

An RNA-dependent DNA polymerase was separated from intact murine leukemia virion by detergent treatment (0.02% Triton X-100) followed by sucrose gradient sedimentation. After a 15 hr banding polymerase activity peaked in the nucleoid region, in the region associated with the whole virion, and in the lighter region of the gradient. Polymerase activity which cosedimented with untreated virus was not inhibited by anti-MSV (murine sarcoma virus) serum, but assays on the treated virus revealed the nucleoid and soluble fractions to be almost completely inhibited by the same rat anti-MSV serum. The specific activity (^3H -thymidine triphosphate incorporated/ μg protein) was 3 times higher in the nucleoid fraction than in the intact virion fraction and soluble fraction from the same gradient, indicating that the DNA polymerase was located in the nucleoid.

- 0590 ABSENCE OF ALKALINE PHOSPHATASE IN RAT THYMIC LYMPHOMA INDUCED BY MURINE LEUKEMIA VIRUS. (E.) Doell, R. G. (Stanford U. Sch. Med., Calif.) and B. J. Mathieson. *Cancer Res* 30(10):2456-2457, 1970.

Mice and rats received intrathymic injections of a murine leukemia virus followed 1 wk later by 100 rads of whole-body X-irradiation, and the resulting thymic lymphomas were sectioned and the sections tested for alkaline phosphatase activity. In mice, after latent periods of from 4.2-5 months tumor incidence ranged from 89-100%, and alkaline phosphatase activity was found in the plasma membranes of 5/11 to 18/26 of tested mice tumors (an incidence of about 60%). In rats, tumor incidence after 4 months was 100% and alkaline phosphatase activity was negligible. Whether or not alkaline phosphatase activity in thymic lymphoma cells is intimately related to the neoplastic transformation process is unclear; however, the data suggest that alkaline phosphatase activity is an incidental occurrence, not related to transformation.

- 0591 CHROMOSOMES OF THE MURINE LEUKEMIA VIRUS INDICATOR CELL LINE XC. (E.) Nelson-Rees, W. A. (U. California, Oakland). *Chromosoma* 31(1):51-60, 1970.

Karyotype analyses were performed on cells derived from tumors induced in rats by Rous sarcoma virus. Cells were hypodiploid, having 41 chromosomes and stem lines existing in the range of diploidy at 40-42 chromosomes. The longest chromosome was subtelocentric and often exhibited 2 or 3 secondary constrictions. Tumor cells had approximately 18 size-graded metacentric chromosomes and 1 pair of subtelocentric chromosomes. Unconventional chromosomes which did not resemble those ordinarily found in *Rattus norvegicus* consisted of about 7 size-graded, 2-armed chromosomes which were significantly smaller than the next largest chromosomes.

- 0592 LEUKEMOGENIC ACTIVITY OF THE RADIATION INDUCED LEUKEMIA VIRUS OF THE MOUSE. (Fr.) Duplan, J. F. (Curie Found., Paris, France), P. Monnot and P. B. Mistry. *Bull Cancer* 57(1):23-30, 1970.

The presence of a leukemogenic virus in normal mouse spleen extracts prepared from C57BL male female animals 300-500 days old was established. Acellular spleen extracts (Tyrode's solution) were injected into 31 one-month-old isogenous healthy mice (0.2 ml, i.p., once or twice) and to 28 mice the same age group exposed to whole body irradiation following inoculation (175 rad, 2-4 times at weekly intervals, starting at age 40-45 days). Irradiated animals were treated i.v. with 7×10^6 - 10^7 cells of isogenous bone marrow 4 hr before or 24 hr after the last exposure. Leukemia developed in 48% of nonirradiated, in 45% of the irradiated and in 100% of the control (nontreated) animals. Of these, 11 tumors (lymphoreticuloses) appeared in 11 out of 28 nonirradiated, spleen extract-inoculated mice, 10 out of 28 irradiated and inoculated mice. These tumors were not transplantable when inoculated or i.p. to isogenous young animals; however, 5 tumors developed in 50% of these animals 300-600 days after tumor inoculation. Irradiated animals developed transplantable lymphosarcomas of the thymus at days.

- 0593 INTRACISTERNAL A-TYPE PARTICLES IN MURINE NEOPLASIAS WITH AND WITHOUT PARAPROTODERMIC PRODUCTION. (E.) Ebbesen, P. (Inst. Tumor Virus Res., U. Copenhagen, Denmark) and M. H. Nielsen. *Acta Path Microbiol Scand* 78(3):390-394, 1970.

Tissue blocks prepared from the peripheral lymph nodes, spleen, and thymus of mice bearing immunoplasma cell neoplasias induced by subcutaneous injection of murine leukemia virus were examined electron microscopically to locate virus-like particles. A-type particles located in the cisternae of the endoplasmic reticulum and in the perinuclear space were the virus-like particles observed; these particles averaged 70 m μ in transverse diameter. They showed 2 electron-dense shells around a 30 m μ wide electron-translucent core. In most instances the particle surface was covered by a layer of granular material with moderate electron-density. A few electron-dense granules were noted in the core of some A-type particles. The A-type particles apparently were formed by inward budding from the membrane of the endoplasmic reticulum, and occurred whether or not the neoplasm produced paraproteins.

- 0594 GENETIC SUSCEPTIBILITY TO LEUKEMOGENIC INTRATHYMIC INOCULATION OF CELL-FREE SUPERNATANTS OF THE THYMUS FROM FIVE-MONTH-OLD, NONLEUKEMIC AKR MICE. (E.) Nakakuki, K. (Sch. Med. Prefect. U., Japan). *Gann* 61(4):393-396, 1970.

Cell-free supernatants from thymus preparation from 5 month-old grossly non-leukemic AKR mice were inoculated into the thymus of 10-15 day-old mice (AKR/Ms, C3Hf/Bi, C57BL, A/Jax, DBA/2, (C3Hf x C57BL)F₁, and (C57BL x ARR)F₁), in amounts ranging from 0.02-0.03 ml/mouse, for the purpose of investigating the incidence of leukemia development in tests with different inherited susceptibility to leukemia. Leukemias which developed were all thymic lymphomas with or without hepatosplenomegaly and lymph

involvement. The incidence of leukemia was 100% in mice of strain AKR, C3Hf, and (C3Hf x AKR) F_1 . However the latent period of leukemia development varied greatly in these 3 strains, with AKR and (C3Hf x AKR) F_1 strains showing short latencies (56 and 67 days, resp.), and C3Hf showing a latency ranging from 72-200 days. Mice of other strains except C57BL showed lower leukemia incidences, but in no case was the incidence insignificant, since all these strains had naturally very low incidences of spontaneous leukemias.

95 INVESTIGATION OF IMMUNIZING PROPERTIES AS WELL AS INTERFEROGENICITY OF SOME MURINE LEUKEMIA VIRUSES. (E.) Mazurenko, N. P. (Acad. Med. Sci., USSR, Moscow) and E. S. Revazova. *Arch Schwulstforsch* 35(4):308-314, 1970.

Mice were inoculated with vaccines prepared from Friend, Rauscher, and Mazurenko virus inactivated with formalin (3 doses of 0.3 ml, i.p., at weekly intervals) to determine if these viruses could produce antibodies not only to homologous virus but to the other viruses. Only in the instance of vaccination with inactivated Friend virus was immunization observed; challenge with Friend virus 3 wk after termination of vaccination resulted in only 10% mortality compared to 97% mortality in controls. Rauscher and Mazurenko inactivated viruses did not protect against homologous virus challenge, and none of the vaccines immunized against any of the other viruses, even when adjuvant was employed. However, with adjuvant, both Friend and Rauscher vaccines protected against homologous virus challenge. Vaccination of mice with combined Friend and Rauscher vaccines produced resistance to the Rauscher virus. Friend virus inactivated with formalin induced the production of interferon in mice susceptible to this virus.

96 GROUP-SPECIFIC ANTIGEN OF MURINE LEUKEMIA VIRUSES IN MICE OF LOW-LEUKEMIC STRAINS. (E.) Abelev, G. I. (N. F. Gamaleya Inst. Epidem. Microbiol., Moscow, USSR) and D. A. Elgort. *Int J Cancer* 6(2):145-152, 1970.

The presence of a group-specific antigen of murine leukemia viruses in mice of low leukemic strains, and in other mice and rats, was investigated. Mice of varying strains, leukemic mice, mouse embryos, and rats bearing Moloney rat sarcoma were used as tissue donors, and tissue cultures were exposed to rabbit monospecific anti-murine leukemia virus group-specific antigen antiserum used for detection of the antigen. An indirect immunoradiography technique was used in the analyses of the tissue cultures for antigen to permit the detection of trace amounts of antigen. Anti-murine leukemia virus group-specific antigen was found in all mouse strains, both high- and low-leukemic; AKR strain mice had the highest levels of antigen, and C57BL/6 and B10D2 had the lowest. Highest levels of antigen generally were found in spleen and thymus of embryos of C57BL/6 and BALB/c strain animals. No antigen could be found in the spleens of newborn or

adult rats; however, antigen was present in high amounts in rats with sarcomas induced by Moloney virus.

0597 PREVALENCE OF MURINE C-TYPE RNA VIRUS GROUP SPECIFIC ANTIGEN IN INBRED STRAINS OF MICE. (E.) Myers, D. D. (Jackson Lab., Bar Harbor, Me.), H. Meier and R. J. Huebner. *Life Sci* 9(18):1071-1080, 1970.

Sera from mice bearing C-type virus-induced tumors were subjected to the complement fixation test for the detection in these sera of group-specific antigen to murine C-type RNA virus. The group-specific antigen was detected in 80% of high-leukemia strains of mice (AKR/J, C58/J, SJL/J), 41% in intermediate-leukemia strains (RF/J) and 23% in low-leukemia strains (A/HeJ, A/J, BALB, CBA/J, C3HeB/FeJ, C57BL/6J, C57BL/10J, C57BR/cdJ, C57L/J, DBA/2J, SWR/J). The prevalence of antigen increased with age in most strains, and genetically related strains had a similar incidence. Apparently, endogenous-physiological factors such as age, and exogenous environmental factors can modify the patterns of virus expression, although that pattern is partially genetically determined.

0598 IMMUNOFLUORESCENT STUDY OF THE GROUP-SPECIFIC ANTIGEN OF MURINE LEUKEMIA VIRUSES. (E.) Lejneva, O. M. (N. F. Gamaleya Inst. Epidem. Microbiol., Moscow, USSR) and G. I. Abelev. *Int J Cancer* 6(2):153-159, 1970.

Monospecific antibodies to the group-specific antigen of the murine leukemia viruses were obtained using a new method in normal and malignant tissue. That the reaction was specific for murine leukemia virus antigen was confirmed by the specific inhibition of immunofluorescence after neutralization of the antibodies by partially-purified murine leukemia group-specific antigen. Indirect immunofluorescence demonstrated antibodies in Rauscher leukemic spleen cells of BALB/c mice (100% of mice tested were positive for antibodies) and in normal spleen cells of high-leukemic and some low-leukemic mice. The murine leukemia virus group-specific antigen was shown in cells of methylcholanthrene-induced sarcomas and in cells of tumors induced with polyoma virus (100% antibody positive). The murine leukemia virus group-specific antigen was not seen in III Af mouse sarcoma induced by Rous virus. In general, agar precipitation analysis of tissues gave the same results as immunofluorescence.

0599 CYTOTOXICITY *IN VITRO* OF PRELEUKAEMIC LYMPHOID CELLS ON SYNGENEIC MONOLAYERS OF EMBRYO OR THYMUS CELLS. (E.) Wahren, B. (Karolinska Inst., Stockholm, Sweden) and D. Metcalf. *Clin Exp Immun* 7(3):373-386, 1970.

The syngeneic or autoimmune reactivity of lymphoid cells from 2 high leukemic mouse strains (AKR and the C3H strain carrying Moloney virus) were tested on monolayers of syngeneic embryo and thymus target

cells *in vitro* to determine the importance of immunological reactions in the pathogenesis of leukemia. Cytotoxic reactivity was observed with lymphoid cells of AKR animals aged 3-36 wk (lesions in 16 out of 24 tests) and of C3H animals aged 3-8 wk (lesions in 10 out of 11 tests), but not in younger AKR animals (less than 3-wk-old), and low leukemic strains (C3H/BI and DBA/2 mice). Lymphoid cells from leukemic AKR mice showed reduced activity with lesions occurring in the embryo target cells in only 1 out of 6 tests. Target AKR and C3H-Moloney embryo monolayers contained little virus-induced G+ or M+ antigen, and target embryonic cells preincubated with antiserum directed against AKR G+ cells exhibited reduced cytotoxic effects. Assuming these cytotoxic reactions are genuine immunological responses, they may explain a secondary damage of virus-modified cells in neoplastic transformation by leukemia viruses; alternatively, they may indicate that AKR and C3H-Moloney mice are not completely tolerant to viral-induced antigens, explaining the long pre-leukemic period in these animals.

- 0600 EFFECT OF CONCURRENT MALARIAL INFECTION ON DEVELOPMENT OF VIRUS-INDUCED LYMPHOMA OF BALB/c MICE. (E.) Wedderburn, N. (Roy. Coll. Surg., London, England). *Lancet* 2(7683):1114-1116, 1970.

The effect of concurrent infection with *Plasmodium berghei yoelii* (Pby, 10^6 cells, i.p.) on the oncogenicity of Moloney leukemogenic virus (0.5 ml of a 20% extract, i.p.) was determined by the incidence of malignant lymphoma in host BALB/c mice. Only 1 out of 11 mice injected with the virus developed lymphoma (latent period of 20 weeks), while none of the 10 mice receiving Pby showed evidence of lymphoma after 6 months. Of the 12 mice injected with both agents within 5 min of each other, 10 showed signs of generalized lymphoma after 15-24 wk; and of the 13 mice receiving Moloney leukemogenic virus 10 days after Pby, 6 showed signs of lymphoma 15-26 wk after receiving the virus. A synergistic effect is suggested in the animals receiving Moloney leukemogenic virus with or after Pby.

- 0601 RNA SYNTHESIS IN NUCLEI ISOLATED FROM NORMAL AND FRIEND VIRUS-INFECTED MOUSE SPLEEN. (E.) Munson, B. R. (Roswell Park Mem. Inst., Springville, N. Y.), R. J. Fiel and J. L. Ambrus. *Cancer Res* 30(9):2414-2419, 1970.

RNA synthesis in the nuclei of spleen cells from normal mice and mice infected with Friend virus was assayed by measuring the amount of ^{14}C -ATP incorporated into a cold acid-insoluble residue. Nuclei from virus-infected spleen contained 2.8 times as much RNA as nuclei from normal spleen (RNA/DNA ratios of 0.627 and 0.225, resp.) Optimal reaction conditions for RNA polymerase activity at high and low ionic strengths were similar in normal and in virus-infected rat liver nuclei, except that a typically bell-shaped curve for the pH optimum was not obtained for the enzyme in the normal nuclei while the RNA polymerase activity of both normal and

Friend virus-infected nuclei was stimulated at low ionic strength, the level of activity in the spleen from virus-infected spleen cell was 4 times greater than in normal spleen cells. The differential response of RNA polymerase activity in normal spleen cells to high and low ionic strengths suggests that a factor other than the related DNA template activity is involved in the RNA polymerase activity found in metabolically stimulated tissues.

- 0602 ENHANCEMENT OF FRIEND LEUKEMIA VIRUS INFECTION IN MICE BY GUAROA VIRUS: QUANTITATION AND ACTION OF VARIOUS ONCOGENIC AND NON-ONCOGENIC VIRUSES. (E.) Spahn, G. J. (Nat'l. Inst., Nat'l. Inst. Hlth., Bethesda, Md.), W. R. L. Peters and M. A. Chirigos. *Appl Microbiol* 20(4):551-554, 1970.

The enhancement by guaroa virus of virus infection by Friend leukemia virus (FLV) was investigated in mice. Male mice from 6-8 wk old were given inoculations of guaroa virus in amounts of 4 LD₅₀ for suckling mice, followed 3 days later by infection with FLV in concentrations of 200 spleen-enlarging doses. Spleen-foci activity, spleen wt, and amount of infectious virus recoverable from plasma were markedly increased by infection with guaroa virus and FLV. Spleen in co-infected mice showed a more than 2-fold increase over mice infected with FLV only with receiving FLV at 200 spleen-enlarging doses. 74 spleen foci 7 days after infection and mice receiving both FLV and guaroa virus showing about 100 foci. Co-infected mice had mean spleen wts of 100 mg when infected with 20 spleen-enlarging doses of FLV, while mice receiving only this amount of FLV had a mean spleen wt of 100 mg. In plasma preparations of FLV alone, recoverable virus was barely detectable, whereas in co-infected mice there was a nearly 75-fold increase of infectious virus recovered. Co-infection of vesicular stomatitis virus and FLV produced a significant increase in spleen foci, but the increase did not approach that achieved with guaroa virus.

- 0603 FURTHER STUDIES ON THE BIOLOGICAL RELATIONSHIPS OF FRIEND VIRUS-INDUCED LEUKEMIC CELLS DIFFERENTIATING ALONG THE ERYTHROCYTIC LINE. (E.) Rossi, G. B. (Higher Inst. Sanit., Rome, Italy) and C. Friend. *J Cell Physiol* 76(2):171-179, 1970.

Replication and erythroid differentiation of Friend virus-induced leukemic cells were studied. Cells were injected i.v. into young mice before and after the second of 2 doses of X-radiation (950 r or 1200 rads, resp.). The forming unit (CFU) in the recipient spleens was 7-fold higher when injected before irradiation than the CFU obtained when the second radiation had been given shortly after the inoculation of cells. Serial passage of the cells from the colonies to irradiated hosts resulted in a marked increase of the CFU value, indicating that

population was capable of both self-replication and erythroid differentiation. The percentage of the inoculated cells reaching the spleen in the irradiated recipients was found to be approximately 15%. If the highest CFU value obtained from serial colony-to-colony passages is corrected by this factor, a final cloning efficiency of about 18% is demonstrated. Neither induced plethoria nor the administration of erythropoietin (1 U/mouse for 2 days) appeared to affect the spleen colony-forming ability of the leukemic cells. Erythroid differentiation is not detectable in the transplantable subcutaneous tumors which were used to initiate the tissue culture lines and which also are capable of inducing erythroid spleen clones in irradiated recipients. The theory that so-called microenvironmental factors influence the fate of stem cells with potential for differentiation may be supported by the lack of erythroid differentiation in these cells.

0604 ROLE OF RADIATION IN VIRAL LEUKEMOGENESIS. (E.) Yokoro, K. (Res. Inst. Nucl. Med. Biol., Hiroshima U., Japan) and N. Imamura. *Acta Haemat Jap* 32(4):620-628, 1970.

Male and female (Wistar/Furth) rats received 600 rads of total body X-irradiation in 4 doses of 150 rads at 5-day intervals followed by i.p. inoculation of 0.4 ml Gross leukemia virus; other rat groups received X-irradiation or virus inoculation alone. The aim was to investigate the possible synergistic action of total body X-irradiation and viral induction of leukemia in rats. Leukemia was not observed in rat groups which had received X-irradiation at 4-5 wk of age alone or in groups treated 8 wk of age with virus alone; however, the rats receiving combined treatment showed 55% leukemia induction with a latency of 77-213 days. Rats inoculated with virus alone at 2 days of age showed 100% leukemia induction. When cell-free filtrates made from lymphomas induced by the combined treatment were inoculated in newborn rats thymic lymphoma resulted in 13/14 of recipients. To test the effect of Gross virus on the immunological reactivity of the host during incubation, highly susceptible Sprague-Dawley rats were inoculated i.p. with 0.1 ml of the virus shortly after birth, and subsequently they were challenged with sheep red blood cells. Counts of plaque-forming cells in the spleen and mesenteric nodes of control rats showed that plaque-forming cells in spleen and nodes increased progressively while plaque-forming cells in virus-inoculated rats showed no increase. These results suggest that Gross virus induces in the susceptible host a state of immunological suppression well before the development of leukemia. The overall findings suggest that a synergistic action of irradiation and Gross virus is necessary for the induction of leukemia in young rats which are refractory to a single application of either agent.

0605 CELL-FREE TRANSMISSION OF MURINE MYELOID LEUKAEMIA. (E.) Tanaka, T. (Sch. Med. U. Leeds, England) and A. W. Craig. *Europ J Cancer* (4):329-333, 1970.

Liver and spleen extracts from mice having myeloid leukemia induced by radiation were centrifuged, and the resultant supernatant was injected i.v. into 1-3.5 month old mice at doses of 0.2-0.3 ml/mouse to determine if cell-free extracts prepared from leukemic organs would enhance the induction of murine myeloid leukemia. The incidence of myeloid leukemia following injection of supernatant was 38% with an average latency of 37 days. Filtration of the supernatant through Millipore filters of 0.45 or 0.8 μ porosity completely eliminated the infectivity of the supernatant; extraction of the filter with Hank's solution and inoculation of this wash into mice resulted in the development of leukemia in 2 of 6 animals. A filtrate prepared using 3.0 μ membrane filter and physiological saline was a suitable way of enhancing virus yields; 9 mice treated with such a filtrate all developed myeloid leukemia with a latency of 15-20 days. The results clearly indicate that variable numbers of virus particles were held on the filter surface or inside the filter pores, depending both on the medium used for organ extracts, and on the quality and porosity of the filters.

0606 DEMONSTRATION OF BIOLOGICAL ACTIVITY OF A MURINE LEUKEMIA VIRUS OF NEW ZEALAND BLACK MICE. (E.) Levy, J. A. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and T. Pincus. *Science* 170(3955):326-327, 1970.

A hamster tumor cell line transformed by Moloney sarcoma virus (10^5 cells) were cocultivated with embryo cells from BALB/c, NIH and the New Zealand Black mouse strain, in an attempt to demonstrate biological activity of murine leukemia virus in the latter cells. No focus-forming virus was released by hamster tumor cells when cocultivated with BALB/c or NIH cells or when the hamster tumor cells were infected with Rauscher murine leukemia virus; however, when Rauscher murine leukemia virus was added to cultures containing both hamster tumor cells and mouse cells, a focus-forming pseudotype virus was produced. Focus-forming virus was also produced by cocultivation of hamster tumor cells with New Zealand Black mouse cells, demonstrating the existence of murine leukemia virus in the latter cells. The titer of the New Zealand Black mouse-rescued sarcoma virus ranged from 5-100 focus-forming units/0.5 ml cocultivation fluid. The rescued virus presumably carried the New Zealand Black mouse leukemia virus coat.

0607 FREE AND MEMBRANE-BOUND POLYRIBOSOMES IN NORMAL AND RAUSCHER-VIRUS-INFECTED MOUSE SPLEEN CELLS. (E.) Burghouts, J. T. M. (Dept. Biochem, U. Nijmegen, Netherlands), A. L. H. Stols and H. Bloemendal. *Biochem J* 119(4):749-756, 1970.

The influence of Rauscher virus infection on polyribosome profiles was studied by isolating free and membrane-bound polyribosomes (in the presence of ribonuclease inhibitor to prevent degradation) and ribosomal monomers from normal and infected mouse spleens on discontinuous sucrose density

gradients. Leukemic infection increased RNA (mg RNA/mgDNA/g spleen) from both free (14.76 to 28.07) and membrane-bound polyribosomes (1.78 to 5.15) and produced an increase in spleen wt with a shift towards larger polyribosomal aggregates (electron micrographs revealed as many as 40 monomers/polyribosome). Sodium deoxycholate treatment (0.5%) of the membrane-bound polyribosomes from both normal and infected spleens before application to a continuous sucrose density gradient resulted in an increase of only 80 S particles (even in the presence of the ribonuclease inhibitor), suggesting that only the monomers are bound to membranes or that the solubilization by deoxycholate degraded the polyribosomes.

0608 AEROSOL TRANSMISSION OF RAUSCHER MURINE LEUKEMIA VIRUS. (E.) McKissick, G. E. (Vetr. Path. Lab., Merck & Co., Rahway, N.J.), R. A. Griesemer and R. L. Farrell. *J Nat Cancer Inst* 45(4):625-636, 1970.

Weanling mice were exposed to an aerosol of Rauscher murine leukemia virus (retained pulmonary dose of 2675 LD₅₀), with the result that 39.5% of aerosol-exposed mice developed leukemia during an observation period of 25 months from initial treatment. Mice in contact with aerosol-exposed cagemates also developed leukemia, indicating that horizontal transmission of Rauscher murine leukemia virus can occur. The leukemic response of the exposed mice was characterized by a diffuse neoplastic infiltration of the spleen and liver and dissemination of leukemic cells in the circulatory vascular system. These characteristics distinguished the response to Rauscher murine leukemia virus from a spontaneous, aleukemic, multifocal, splenic reticulum cell sarcoma which occurred in aged survivors. The finding that aerosols of a leukemogenic virus are infectious suggests that laboratory infection represents a potentially hazardous form of occupational exposure.

0609 HISTOPROLIFERATIVE EFFECT OF RAUSCHER LEUKEMIA VIRUS ON LYMPHATIC TISSUE: III. ALTERATIONS IN THE THYMIC-DEPENDENT AREA INDUCED BY THE PASSENGER LACTIC DEHYDROGENASE VIRUS. (E.) Snodgrass, M. J. (Oak Ridge Natl. Lab., Tenn.) and M. G. Hanna, Jr. *J Nat Cancer Inst* 45(4):741-759, 1970.

The destruction of small lymphocytes in the thymic-dependent region of lymphoid tissues of mice infected with Rauscher leukemia virus associated with a passenger lactic dehydrogenase virus (LDV) was investigated. Mice were given i.p. injections of Rauscher leukemia virus or LDV in doses of 10,000 or 10⁸ ID₅₀, resp.; spleens were subsequently removed and inspected microscopically with specific attention given to splenic lymphoid nodules. The presence and replication of LDV in the thymic-dependent area were confirmed. Morphologically typical LDV particles were localized intercellularly and in single membrane-bound vesicles of phagocytic reticular cells in the marginal zone at the earliest

intervals after inoculation with Rauscher leukemia virus and/or LDV, corresponding to the well-known events of the exponential phase of the plasma viremia. LDV particles were first seen in the thymic-dependent area, where they were associated with similar phagocytic reticular cells, 24 hr after inoculation. Complete intercellular virus particles were observed throughout the experiment, and incomplete intracellular particles were not present. The virus population in this region increased until day 2, when cellular necrosis and macrophage infiltration were at a peak. On day 4 these effects were cleared, leaving the prominent reticulum, and very few virus particles were present. Although lymphocytes of thymic origin were adversely affected, the result of LDV infection, phagocytic reticular cells in the marginal zone and thymic-dependent area appeared to be the target cell of this virus. The importance of cell-mediated immunity, which is suppressed by LDV, in the host defense against viral infection is supported by the augmented Rauscher leukemia virus-associated splenomegaly after infection with LDV. A synergistic interaction between the passenger LDV and the Rauscher-virus-induced pathogenic process may be indicated by this phenomenon.

0610 INDUCTION OF LYMPHOMA IN BALB/c MICE BY ROWNSON-PARR VIRUS (RPV). (E.) Carter, R. L. (Chester Beatty Res. Inst., London, England), F. C. Chesterman, K. E. K. Rowson, M. H. Salama, and N. Wedderburn. *Int J Cancer* 6(2):290-303, 1970.

Young adult mice received i.v. injections of 10⁶ of a 1:10 dilution of Rowson-Parr virus; in 1 experiment, animals were killed between 4-48 wk of age, and in another, animals were allowed to live out their life-spans. The oncologic response of the mice developed in 4 stages. In stage I there was initially a short-lived phase of moderate splenic enlargement and reactive hyperplasia which resolved, followed by stage 2 which was characterized by a persistent period of slight splenomegaly and low-grade non-specific reactive hyperplasia; stage III neoplasms occurred in the reticulum of the spleen and in the Malpighian follicles of the spleen and were initially confined to these structures. Later (stage IV) there was progressive replacement of splenic pulp and increasing involvement of lymph nodes, liver and thymus; some animals developed terminal leukemia. Stages III and IV occurred in 45% of all test mice; none of these animals survived for more than a year after infection. Four Rowson-Parr virus-infected mice developed lymphomas and leukemias of other histological types. No reticulum-cell neoplasms were found in the uninjected control animals. Two prominent features of the reticulum cell lymphoma associated with Rowson-Parr virus were the biphasic nature of the host response with respect to time and the lymphoma being preceded by long-sustained reactive changes; reactive and plastic changes arose sequentially in the same organ, and perhaps involved the same cell-type, phagocytic reticulum cells. The thymus is apparently involved until late in the disease course in lymphomas produced by Rowson-Parr virus.

11 MULTIPLICATION OF ADENOVIRUS IN HETERO-KARYOCYTES PRODUCED BY FUSION OF INFECTED PERMISSIVE AND NONPERMISSIVE CELLS. (E.) Weber, J. H. U. Sherbrooke, Quebec, Canada) and S. Mak. *Virology* 42(2):540-543, 1970.

The effect of fusion of permissive and non-permissive cells with inactivated Sendai virus on adenovirus 12 multiplication was investigated. In the first of a series of 4 experiments, BHK₂₁ hamster cells (non-permissive) were pretreated with ³H-thymidine, infected with adenovirus 12 (5 plaque-forming units/cell) and fused with human cells (HEp₂). Neither nuclear inclusion bodies nor virus-antigen were found in the nuclei of the human cells in significant amounts; however tumor antigen was found in 44-51% of the unfused hamster cells. In another experiment the virus-infected heterokaryocytes were disrupted by sonication, and the resulting suspension was assayed for virus capable of inducing tumor antigen in human cells; human cell nuclei resident with an infected hamster cell nucleus positive for tumor antigen yielded less than 0.005 plaque-forming units/cell, whereas human cell nuclei containing adenovirus-induced inclusion bodies produced 25 plaque-forming units/cell. Infectious virus was recovered from polycaryocytes formed from the fusion of adenovirus 12-infected and non-infected HEp₂ cells and from heterokaryocytes formed from the fusion of non-infected BHK₂₁ and infected HEp₂. The presence of HEp₂ cytoplasm or nucleus at the time of infection appears to be necessary for the expression of the viral genome, and it seems that no infectious virus can be recovered from adenovirus 12-infected BHK₂₁ cells even by early fusion with HEp₂ cells.

12 STIMULATORY AND INHIBITORY EFFECTS OF ADENOVIRUS AND SV40 ON VARIOUS VIRUS-RECEPTOR SYSTEMS. (E.) Berman, L. D. (Boston City Hospital) and C. Chany. *Arch Ges Virusforsch* 30(2-3): 23-216, 1970.

Cultures of rat, mouse, chicken embryo fibroblast, and hamster cells were infected with adenoviruses or SV40 (0.1 ml of virus) and the infected cultures were subsequently superinfected with vesicular stomatitis virus (VSV), encephalomyocarditis virus or vaccinia virus in order to study changes in superinfectibility brought about by acute adenovirus or SV40 infection. Infection with these viruses caused marked inhibition of superinfection with VSV, encephalomyocarditis virus, or vaccinia virus, with inhibition most marked with adenovirus infection of mouse cells, where a transitory phase of stimulation was frequently demonstrated immediately after adenovirus infection and where inhibition of superinfection reached 100%. The inhibitory phase usually commenced 2-6 hr after infection and depended on infection with intact virions; the inhibitory substance cosedimented with the virions, was completely inactivated by heating at 56°C for 1/2-1 hr but was unaffected by UV-irradiation (2.6-2.8 x 10⁶ ergs/mm²) and crystalline trypsin (1000 µg/ml). Binding of virus by antiserum did not prevent the inhibition, and inhibition could not be explained

by differences in adsorption, interferon production, chromosome breakage, or the effect of soluble capsid antigens. In contrast to acute adenovirus infection, in which the challenge virus was inhibited, mouse cells showed increased sensitivity to VSV after transformation with SV40.

0613 STRUCTURAL PROTEINS OF ADENOVIRUSES: IV. SEQUENTIAL DEGRADATION OF THE ADENOVIRUS TYPE 2 VIRION. (E.) Prage, L. (Dept. Microbiol., Uppsala U., Sweden), U. Pettersson, S. Höglund, K. Lonberg-Holm and L. Philipson. *Virology* 42(2): 341-358, 1970.

Methods were designed for disintegrating the adenovirus type 2 virion in order to investigate the structural units of the highly purified virus. Degradation procedures included dialysis against Tris-maleate buffers, freezing and thawing, and dialysis with pyridine. Dialysis against Tris-maleate buffers in the pH range 6.0-6.6 resulted in a loss of infectivity and in a quantitative release of pentons from the virions. At room temperature, these pentonless virions rapidly also released 5 or 6 hexons original penton unit. The remainder of the capsid was further disintegrated by repeated freezing and thawing, which released hexons in a non-aggregated form and also a precipitated DNA-protein complex. Two major protein components could be extracted from the latter with mineral acids. Amino acid analysis of these internal DNA complexed proteins revealed that they were highly basic, with an arginine content of 19%. Three or more low-molecular weight antigens distinct from hexon, penton base, fiber, and basic core proteins were also released during this procedure. Pyridine at a concentration of 10% degraded virions by a different pattern; hexons originating from the faces of the adenovirus icosahedron were preserved in groups of 9. Peripentonal hexons, fibers, degraded vertex capsomers, and low molecular weight antigens were also released. Eight or more antigenically distinct proteins were distinguished as components of the virion; the internal core of the virus, which was retained in a suspended state contained 15% of the total virion protein.

0614 PARTIAL CHARACTERIZATION OF THE COMPLEMENTARY SITES INVOLVED IN THE REACTION BETWEEN ADENOVIRUS TYPE 7 AND ERYTHROCYTE RECEPTORS. (E.) Neurath, A. R. (Wyeth Lab., Philadelphia, Pa.), R. W. Hartzell and B. A. Rubin. *Virology* 42(3):789-793, 1970.

The sites of interaction of adenovirus type 7 and rhesus monkey RBC were partially characterized by *in vitro* incubation with selective enzymes and chemicals. The adsorption of virus to RBC and the hemagglutination by dodecans were independent of pH, indicating that the α-amino groups (α-NH₃⁺) were not essential to the interaction; since carboxypeptidase B (12.5 µg/ml) and leucine aminopeptidase (110 µg/ml) failed to affect the adsorption to RBC, the terminal amino acid residues of the polypeptides were also not necessary to the ad-

VIRAL CARCINOGENESIS

sorption process. Studies with 2,3-butanedione (a reagent that selectively modifies the arginine residues in proteins) showed that the adsorption and hemagglutination abilities of the virus were destroyed in its presence, although addition of the butanedione to already adsorbed adenovirus did not release the virus from the RBC; this suggests that the reagent-sensitive groups are part of the binding site of the virus to cell receptors. RBC treated with 1-cyclohexyl-3-(2-morpholinoethyl)-carbodiimide metho-*p*-toluenesulfonate (CMC, a reagent that selectively modifies carboxyl groups in proteins) exhibited diminished adsorption capacities to adenovirus (although influenza virus remained agglutinable, indicating that neuraminic acid residues were not altered). RBC already adsorbed to adenovirus were released with CMC treatment, suggesting that the adsorbed virus did not protect the cell receptor sites. The reversible interaction of adenovirus type 7 with RBC receptors apparently requires nonterminal arginine residues in the virus and β - or α -carboxylic acid residues in the RBC membrane protein.

- 0615 TRANSFORMATION OF HAMSTER CELLS BY VARIANTS OF PARA-ADENOVIRUS 7 ABLE TO INDUCE SV40 TUMOR ANTIGEN IN THE CYTOPLASM. (E.) Duff, R. (Milton S. Hershey Med. Ctr., Pennsylvania St. U., Hershey), F. Rapp and J. S. Butel. *Virology* 42(1): 273-275, 1970.

Cultures of hamster embryo fibroblast cells were exposed to 1 of 3 strains of cytoplasmic hybrid virus (1cT, 2cT, 3cT) SV40 (PARA) and adenovirus type 7 hybrid (SP2) in order to investigate the transformation of the cells by these virus strains (1 ml of virus-containing fluid was adsorbed in 8×10^5 cells). Virus strain 2cT transformed fibroblasts at a frequency 3-6 times greater than the transformation frequency of the other strains (7.0 focus-forming units/plate examined); however, none of the strains transformed cells at a frequency equal to that of the parental SP2 stock of hybrid virus (which transformed at a rate of 10.25-36.25 focus-forming units/plate examined). Fibroblasts transformed by hybrid virus contained nuclear SV40 tumor antigen. A transformed focus of fibroblast was grown as a cell line, and its oncogenic potential was tested by injecting transformed cells s.c. into hamsters; tumors were induced in 6/17 of the hamsters injected.

- 0616 SPECIFIC ANTITUMOR IMMUNITY INDUCED WITH ADENOVIRUS SA7(C8)-INFECTED CELLS IN HAMSTERS. (Rus.) Babakova, S. B. (P. A. Hertsen Res. Inst. Oncol., Moscow, USSR). *Vop Onkol* 16(6):69-73, 1970.

Specific antitumor immunity in hamsters was induced under 3 sets of experimental conditions: I) by i.v. inoculation of adenovirus type SA7(C8)-induced tumor cells (1 ml of a suspension containing 10^6 cells twice and 10^7 cells once at 7 day intervals); II) i.v. inoculation of freeze-thawed tumor

cells (frozen at -70°C and thawed at room temperature) or ^{60}Co -irradiated tumor cells (5000 rad 36.5 min, single dose) once or 3 times as above and III) i.v. inoculation of adenovirus type SA7(C8)-contaminated embryonic fibroblastic cell cultures (1 ml of suspension containing 5×10^6 cells for 3 times). Antitumor immunity was tested by challenge with a s.c. transplant of a tumor producing amount of SA7 or SV-40 virus induced tumor cells. Specific antitumor immunity was obtained by inoculation with SA7(C8) adenovirus-transformed cells, with irradiated tumor cells and with virus-contaminated cell tissue cultures; no such immunity was produced by freeze-thawed tumor cells. The data seem to indicate the presence of a specific virus-induced transplantation antigen within transformed or contaminated cells.

- 0617 INTERACTIONS BETWEEN SENSITIZED LYMPHOCYTES AND ADENOVIRUS-12-INDUCED TUMOR CELLS. (E.) McDougall, P. T. (Baylor Coll. Med. Houston, Tex.), G. L. Van Hoosier, Jr. and J. Trentin. *Tex Rep Biol Med* 28(1-2):75-86, 1970.

Hamsters were administered increasing sensitive doses of 4-6 i.p. injections of cells derived from adenovirus type 12 tumors, or of cell suspensions prepared from primary or transplant hamster tumors induced by adenovirus type 12; thereafter, sensitized hamsters were killed, and spleen cell preparations were made to determine whether spleen lymphoid cells from immunized animals exert a detrimental effect on the growth of adenovirus-12 induced tumor cells in newborn hamsters. The growth of tumor cells was inhibited when inoculated together with spleen cells from immunized animals, shown by a decreased percentage of tumor take, by a delay in time of appearance of tumors subsequent to inoculation. Of 9 animals inoculated with only tumor cells and 2 animals inoculated with tumor cells plus normal spleen cells, all developed tumors in 20-25 days; of 8 animals inoculated with tumor cells plus immune spleen cells, only 3 developed tumors within 20-25 days and after 8 weeks one other hamster also developed tumors. No antitumor activity of sensitized spleen cells against adenovirus-induced hamster tumors was observed *in vitro*.

- 0618 IMMUNOLOGICAL ANALYSIS OF HAMSTER SARCOMA INDUCED BY ADENOVIRUS TYPE 12. (Rus.) Bashkaev, I. S. (P. A. Herzen Res. Inst. Oncol., Moscow, USSR), A. I. Ageenko and E. Sh. Vardosanidze. *Vop Onkol* 16(7):60-61, 1970.

Immunodiffusion methods revealed 3 distinct precipitin arcs for antigens contained in adenovirus-12-induced hamster sarcoma: 1 arc was in the region of fast α_1 -globulin and 2 arcs were in the region of γ -globulins. The antigens of the first arc and one of the γ -globulin regions were serologically identical to the normal lung tumor antigens; the other antigen of the γ -globulin region was a specific sarcoma tissue antigen. The arcs noticed in the β -globulin region were

identified. The difference between the normal lung tissue antigen and the antigen of the sarcoma tissue seemed to be a quantitative rather than a qualitative one, possibly associated with the activation of certain parts of the cell gene during virus-induced tumorigenic transformation.

- 0619 MORPHOLOGICAL CONFIRMATION OF THE HERPES NATURE OF A CARCINOGENIC VIRUS OF PRIMATES (HERPES SAIMIRI). (E.) Morgan, D. G. (U. Bristol Med. Sch., England), M. A. Epstein, B. G. Achong and J. V. Melendez. *Nature* 228(5267):170-172, 1970.

Confluent owl monkey kidney cell cultures were infected with sufficient virus tentatively designated *herpes saimiri* to produce moderately widespread cytopathic change; infected cells were prepared for electron microscope examination in order to classify the virus definitively. All the infected cultures contained profuse virus particles of herpes-type morphology. In thin sections immature hexagonal particles, either empty or with central ring-shaped or dense nucleoids and of about 108 nm diameter, were seen in both nuclei and cytoplasm. Mature particles with an additional enveloping membrane measured 140 nm across and lay in the perinuclear space, in cytoplasmic spaces or close outside the cell surface. Morphologically, *Herpes saimiri* appears to be a member of the herpesvirus group.

- 0620 CELLULAR CHANGES OF NORMAL HUMAN CERVICAL EPITHELIUM INFECTED *IN VITRO* WITH HERPESVIRUS HOMINIS, TYPE TWO (HERPES SIMPLEX). (E.) Albanks, G. D. (Rush Med. Coll., Chicago, Ill.), J. A. Campbell and L. A. Kaufmann. *Acta Cytol* 14(4):538-543, 1970.

Cellular changes of normal human cervical epithelium were observed with time lapse cinematography after infection *in vitro* with herpesvirus hominis, type two (herpes simplex) obtained from lesions of a patient with genital herpes. The first changes observed (after 6-8 hr) in the infected cells were clumping of nuclear chromatin at the nuclear membrane, disappearance of the nucleoli, and an increase in the density of the cytoplasm. Then certain cells showed a cytoplasmic decrease and slowing movements of the cell membrane and cytoplasmic organelles, and finally fused into a multinucleated giant cell (polykaryosome). The similarity of these changes with those observed in Papanicolaou smears from patients with genital herpes suggests that the smear technique can be used for diagnosis of genital herpes and for investigation of a possible correlation between these infections and cervical cancer.

- 0621 CHARACTERIZATION OF THE DNA OF HERPESVIRUSES ASSOCIATED WITH LUCKE ADENOCARCINOMA OF THE FROG AND BURKITT LYMPHOMA OF MAN. (E.) Wagner, E. K. (Dept. Microbiol., U. Chicago, Ill.), B. Roizman, T. Savage, P. G. Spear, M. Izell, F. E. Durr and D. Sypowicz. *Virology* 42(1):257-261, 1970.

DNA was extracted from herpesvirus preparations obtained from a Lucke adenocarcinoma of the frog and Epstein-Barr virus. The frog virus was found in both nuclear and cytoplasmic cellular fractions, appeared to possess 162 capsomeres, and had DNA with a buoyant density of 1.703 g/cm³. DNA purified from human Burkitt's lymphoma herpesvirus showed 3 density pools of 1.716 g/cm³, 1.716 g/cm³ in 2 different centrifuge bands, and 1.695 g/cm³ in 2 centrifuge bands. Approximately 1/3 of the DNA from Burkitt's tumor virus had a density characteristic of human cell DNA and is assumed to be of host origin; the other 2/3 of the DNA had a density of 1.716-1.718 g/cm³ which corresponds to 57-58 mole% of guanine and cytosine and appears to be of viral origin.

- 0622 HERPETIC INCLUSIONS IN THE ENDOMETRIUM. (E.) Goldman, R. L. (Community Hosp., North Hollywood, Cal.). *Obstet Gynec* 36(4):603-605, 1970.

A 29 yr-old woman presenting with probable missed abortion showed evidence of herpesvirus infection of the endometrium. The association of the infection with apparent abortion suggests that infection of the placenta may have resulted from a prior infection of the endometrium. In view of the increasing evidence for a correlation between carcinoma of the cervix and herpesvirus infection, the finding of herpesvirus infection in still another potential site of neoplasia is noteworthy.

- 0623 IMMUNOFLUORESCENT DETECTION OF HERPESVIRUS ANTIGENS IN EXFOLIATED CELLS FROM THE HUMAN CERVICAL CARCINOMA. (E.) Royston, I. (Stanford U. Hosp., Calif.) and L. Aurelian. *Proc Nat Acad Sci* 67(1):204-212, 1970.

Direct and indirect immunofluorescent examination was performed on exfoliated cells from patients with squamous carcinoma of the cervix; exfoliated dyskaryotic cells from patients with invasive and preinvasive cervical carcinoma were found to contain antigens related to those found in cells infected with herpes simplex virus, type 2. Normal squamous cells from the same subjects and from controls without the disease, as well as cells from mammary carcinoma and endometrial carcinoma did not react with anti-herpesvirus subtype 2 serum. No reaction with the exfoliated cells was demonstrated by antisera to adenovirus type 18 or by *Mycoplasma orale*.

- 0624 HERPESVIRUS-TYPE-2 ANTIBODIES AND CARCINOMA OF THE CERVIX. (E.) Rawls, W. E. (Baylor Coll. Med., Houston, Tex.), K. Iwamoto, E. Adam, J. L. Melnick. *Lancet* 2(7683):1142-1143, 1970.

The incidence of antibodies to venereally transmitted herpes virus type 2 in women with invasive cervical cancer and with cervical carcinoma *in situ*

was investigated. Ninety-six patients and 42 control subjects from New Zealand were examined; 31% of the patients with invasive cervical cancer and 32% of the patients with carcinoma *in situ* were found to have virus antibodies in their sera, as opposed to 23% of controls. These findings conflict with reported incidences of 78-100% antibody-positive invasive cervical carcinoma cases reported in other studies. The data suggest differences in the rate of progression from *in situ* carcinoma to invasive carcinoma, and the variations are perhaps associated with differing sexual practices in the tested populations.

- 0625 NASOPHARYNGEAL CARCINOMA (NPC): I. TYPES OF CULTURES DERIVED FROM TUMOR BIOPSIES AND NON-TUMOROUS TISSUES OF CHINESE PATIENTS WITH SPECIAL REFERENCE TO LYMPHOBLASTOID TRANSFORMATION. (E.) De-The, G. (Ctr. Internat. Res. Cancer, Lyon, France), H. C. Ho, H. C. Kwan, C. Desgranges and M. C. Favre. *Int J Cancer* 6(2): 189-206, 1970.

Cell cultures obtained from biopsy specimens of Chinese nasopharyngeal carcinomata were of 4 types: 26% of biopsies produced epithelial growth of short duration (4-12 wk) and of limited extent around the explants; 70% of cultured biopsies produced early lymphocytic production which lasted from 1-3 wk; 76% of cultures produced fibroblastic cultures, either as primary or secondary to the epithelial growth; 28% of cultures exhibited lymphoblastoid transformation resulting in the establishment of long-term, free-floating cell-lines. Most of these latter lines were independent; however, a few were intermittently dependent on the presence of fibroblasts during crises. Biopsy specimens from head and neck tumors other than nasopharyngeal cancer, from hypertrophied and inflamed tonsils removed from children, and from apparently tumor-free nasopharyngeal mucosa gave rise to a similar spectrum of cultures, including the establishment of long-term lymphoblastoid cultures. In 3 out of 4 cases which underwent transformation, the Henle titer of the corresponding sera was low. The various lines thus obtained exhibited the presence of a herpes-type virus. The establishment of permanent lymphoblastoid lines was probably due to the presence, in the original material, of a herpes-type virus with transforming properties. Although there is no evidence to support the hypothesis of a direct causal relationship between herpes-type virus and nasopharyngeal cancer, an indirect causal relationship may exist between them, whereby the virus acts in synergy with environmental carcinogens.

- 0626 ISOLATION AND PROPAGATION OF A VIRUS FROM A SPONTANEOUS MAMMARY CARCINOMA OF A RHESUS MONKEY. (E.) Jensen, E. M. (John L. Smith Mem. Cancer Res., Maywood, N.J.), I. Zelljadt, H. C. Chopra and M. M. Mason. *Cancer Res* 30(9):2388-2393, 1970.

A virus which was detected in a spontaneous mammary carcinoma of a rhesus monkey was isolated, and prop-

agated in various tissue cultures for the purpose of preliminary characterization. The virus particles were morphologically similar to known oncogenic RNA-type viruses. Initial isolation was effected by cocultivation of tumor tissues with monkey embryo cell cultures; however, it was later found that the virus was transmissible as a cell-free filtrate. The virus was approximately 100 mμ in diameter and had a buoyant density between 1.14 and 1.16. Preliminary host range studies showed that the virus replicated in rhesus monkey mixed embryo, embryo lung, chimpanzee lung, and human mixed embryo cell cultures, and in an established human leukocyte culture. The virus did not replicate when introduced into baboon or chimpanzee leukocyte cultures, hamster kidney, mouse bone marrow, or rhesus or African green monkey kidney cells.

- 0627 GENETIC TRANSMISSION OF VIRUSES THAT INDUCE MAMMARY TUMOR IN MICE. (E.) Bentvelzen, J. (Organization Hlth. Res., TNO, Rijswijk, Netherlands), J. H. Daams, P. Hageman and J. Calafat. *Proc Natl Acad Sci* 67(1):377-384, 1970.

Three strains of untreated mice (Gr, C3Hf and BALB/c) and 2 strains of mice pretreated with irradiation (urethane 020 and C57BL) were infected with mammary tumor virus to investigate the genetic transmission of these viruses. In general, the viruses were transmitted vertically by the gametes of the mouse strain in which they naturally occurred. The virus was present in every cell, although often in an incomplete form. If a mammary tumor virus was introduced into a different mouse strain, only milk-borne transmission occurred, after which the virus was found in a limited number of tissues. Mammary tumor viruses may be transmitted as genetic factors of the host strain to which they belong. A repressor, produced by a regulator gene, appears to control the rate of release of such a genetically transferred virus. Repression can be abrogated by a carcinogenic treatment. The repressor would interfere with the replication of a superinfecting mammary tumor virus.

- 0628 MAMMARY TUMORIGENESIS IN SPLENECTOMIZED MICE. (E.) Squartini, F. (U. Pisa Med. Sch., Italy) and G. B. Bolis. *Texas Rep Biol Med* 28(1-2):115-121, 1970.

Female mice of BALB/cf(C3H) and RIII strains were subjected to splenectomy, thymectomy, both operations, or no operation to investigate the effect of splenectomy on mammary tumorigenesis in mice carrying spontaneous mammary tumor virus infection. In BALB/cf(C3H) females, neonatal splenectomy decreased both the incidence and age of onset of mammary tumors from 82% to 52%, and by an average of 102 days, resp. Thymectomy decreased the incidence of mammary tumors (46%) and increased the age of onset by an average of 130 days; splenectomy of previously thymectomized females partially suppressed the effect of thymectomy and restored the pattern of tumor development to that seen in intact controls. No significant effect was noted on mammary tumor

nesis in RIII mice undergoing splenectomy alone associated with thymectomy.

- 29 MAMMARY-TUMOR VIRUS ACTIVITY IN BRAIN AND LIVER OF GR STRAIN MICE. (E.)
ntvelzen, P. (Netherlands Cancer Inst., Amsterdam) and J. H. Daams. *Europ J Cancer* 6(9):273-276, 1970.

11-free extracts of liver and brain of mice (GR strain) carrying mammary tumors induced by mammary tumor virus were injected i.p. into young BALB/c mice (0.5 ml/mouse), and blood from tumor-bearing mice was similarly injected into test mice (0.1 ml/mouse), to investigate the incidence of tumors in injected mice of various strains. Only 1 out of 81 inbred-bred mice of the BALB/c strain developed a mammary tumor before attaining 1 yr-of-age in control animals, but extracts from livers and brains induced 35 and 29% mammary tumors, resp., in these mice. Brain and liver extracts from other mouse strains which carry mammary tumor virus (C3H strain, BALB/cfC3H strain, and BALB/cfGR strain) caused no tumors. Whole blood of mammary tumor virus-carrying mouse strains BALB/cfC3H and BALB/cfGR induced mammary tumors in recipient mice (tumor incidence 75-90%), while blood from virus-carrying strain mice caused only 25% tumor incidence. Liver, brain and blood of virus-carrying GR mice appears to contain a biologically active form of the mouse mammary tumor virus.

- 30 VIRUS PARTICLES IN A TRANSPLANTABLE RAT MAMMARY TUMOR OF SPONTANEOUS ORIGIN. (E.)
opra, H. C. (John L. Smith Mem. Cancer Res., Wywood, N. J.), A. E. Bogden, I. Zelljadt and E. M. Jensen. *Europ J Cancer* 6(9):287-290, 1970.

Male rats were implanted with grafts from a transplantable adenocarcinoma derived from a spontaneous mammary fibroadenoma; graft slices (10 x 10 x 1 mm) were implanted s.c. in the supra-scapular and/or supra-sacral regions, and an electron microscopic search for virus particles was undertaken in the resultant tumors. C-type virus particles measuring 50 mμ were observed. When virus particles were propagated in tissue culture, the cells replicated C-type particles at a greater frequency than the original tumor cells had. Sucrose-density gradient centrifugation of the particles from tumor as well as from tissue culture yielded a large number of virus particles at a buoyant density of 1.14-1.18 g/cm³.

- 31 STRAIN C3H-A^{VY}fB MICE: NINETY PERCENT INCIDENCE OF MAMMARY TUMORS TRANSMITTED EITHER PARENT. (E.) Vlahakis, G. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), W. E. Ston and G. H. Smith. *Science* 170(3954):185-187, 1970.

After nursing and hybridization experiments were performed with strain C3H-A^{VY}fB mice, which are highly susceptible to mammary tumors (incidence approaching 90% by 15 months-of-age), to determine

whether this susceptibility is transmitted in milk via a mammary tumor virus, or in factors transmitted at conception. Reciprocal matings were effected between the susceptible strain of mice, and a strain having a low incidence of mammary tumors. In addition, low-incidence mice were nursed by high-incidence females, to investigate the possibility of milk transmission of a mammary tumor viral agent. The result of reciprocal hybridization between susceptible C3H-A^{VY}fB mice and less susceptible mice gave no evidence of a maternally transmitted agent implicated as the cause of a high incidence of mammary tumors in the former strain; there was a high tumor incidence in both reciprocal groups (highest incidence in the F₁ generation, 96.3%, lowest, 57.9%). There was no evidence of a mammary tumor virus transmitted to unsusceptible mice in the milk of susceptible nursers; tumor incidence in unsusceptible mice so nursed was only 7.7%. It may be that the factor responsible for a high incidence of mammary tumor in C3H-A^{VY}fB mice is the A^{VY} gene, which may increase the virulence or transmissibility of a variety of mammary tumor virus transmitted vertically by either parent.

- 0632 PRESENCE OF A, B AND C VIRUS-LIKE PARTICLES IN ORGANS OF R111/Dm/Se MICE. (It.)
Bucciarelli, E. (Dept. Res. Cancer, U. Perugia, Italy), G. B. Bolis and F. Squartini. *Lav. Anat. Pat. Perugia* 30(2):57-72, 1970.

Electron microscopic investigations of the distribution of viral particles were made in various organs (mammary gland, epididymis, spleen, thymus, bone marrow and lymph nodes) of R111/Dm/Se female and male mice in the following conditions: one 15-month-old virgin female; two 8-month-old lactating females (3rd pregnancy); 7 multiparous females; one 14-month-old leukemic female; and 6 normal males (8-15 month-old). Four types of viral particles were observed: intracisternal A-type particles, C-type particles (leukemia virus), cytoplasmic A-type particles and B-type particles (MTV). The intracisternal A-type particles were present in most of the organs of normal male, normal and leukemic or mammary gland tumor-bearing female mice; larger amounts were found in the thymus, spleen, marrow and lymph nodes of normal males and leukemic females. C-type particles occurred frequently but never in large amounts in the thymus, spleen and lymph nodes of the leukemic virgin female, the normal males, and the tumor-bearing females as well as in the nipples of lactating females. The cytoplasmic A-type particles were found in the lactating nipples, the mammary gland tumors and the epididymal tissues and were constantly associated with B-type particles in the epithelial cells of these tissues. The presence of cytoplasmic A particles in the thymus, spleen and lymph nodes suggested a possible direct replication of MTV in the lymphopoietic organs; this hypothesis was supported by the bud-like accumulations of these particles in the spleen and lymph nodes of mammary gland tumor-bearing animals, resembling the early stages of development of the B particles.

- 0633 STUDIES ON DDD MOUSE WITH SPECIAL REFERENCE TO MAMMARY GLAND TUMORS. (E.) Matsuzawa, A. (Inst. Med. Sci. U. Tokyo, Japan), T. Yamamoto and K. Suzuki. *Jap J Exp Med* 40(3):159-181, 1970.

The incidence of mammary tumors in virgin mice of the DDD strain, the association of viruses with these tumors, and the tumor-bearing status of pregnant and multiparous mice were studied together with other factors implicated in mammary tumorigenesis. Mammary tumors reached maximum development in virgin mice at the age of 6 months, and atrophic changes in these tumors coincided with decreases in the hormone-producing components of the ovaries. Mammary hyperplastic nodules (averaging 2 in number) were found in virgins above 9 months of age with nodules becoming abundant by 15 months. Hyperplastic nodules could be induced by hormonal stimulation (estrogen + deoxycorticosterone) in 5-wk-old mice. Mammary plaques were rare; however, the mice were found to harbor mammary tumor virus and to transmit it to offspring via breast milk. Mammary tumors and neoplasms of reticular tissue occurred at a mean age of 16.4 months in 34.4% of 67 virgin mice. In 2 force-bred strains mammary tumors developed at an incidence of 71.5 and 90%. Mammary tumor virus appeared to be weakly oncogenic in DDD strain mice but strongly oncogenic in strain BALB/cJms mice. All mammary tumors developed were adenocarcinomas.

- 0634 MECHANISM OF CARCINOGENESIS BY RNA TUMOR VIRUSES: I. AN RNA-DEPENDENT DNA POLYMERASE IN MURINE SARCOMA VIRUSES. (E.) Green, M. (St. Louis U. Sch. Med., Mo.), M. Rokutanda, K. Fujinaga, R. K. Rey, H. Rokutanda and C. Gurgo. *Proc Nat Acad Sci* 67(1):385-393, 1970.

Two murine sarcoma viruses were isolated from virus-infected mice and subjected to DNA polymerase assay procedures, with the result that an active and stable DNA polymerase was identified. Treatment of virus preparations with a nonionic detergent (0.01% Nonidet P-40) was necessary for the detection of enzyme activity. The incorporation of labeled thymidine triphosphate required all 4 deoxyribonucleoside triphosphates and either Mg or Mn ion. Enzyme activity was proportional to virus concentration and was linear with time up to 90 min. The pH optimum for the enzyme was 8.1, and maximal activity was seen at 37°C. The reduction in polymerase activity upon treatment of murine sarcoma virus with RNase, and the absence of detectable amounts of DNA in the virus suggested that the template was RNA. All 4 deoxyribonucleoside triphosphates were incorporated into an acid-insoluble product which was stable in alkali destroyed by DNase, sedimented in alkaline sucrose gradients with a sedimentation coefficient of 7 S, and banded in isopycnic CsCl gradients with a mean buoyant density of 1.700. These findings indicate that the product of the enzyme is DNA.

- 0635 IMMUNITY TO MURINE SARCOMA VIRUS (MSV)-INDUCED TUMORS DEMONSTRATED BY *IN VIVO* ELIMINATION OF ⁵¹CHROMIUM LABELED TUMOR CELLS. Burstein, N. A. (Massachusetts Gen. Hosp., Boston). *Europ J Clin Biol Res* 15(8):873-875, 1970.

Immunity to murine sarcoma virus (MSV)-induced tumors (⁵¹chromium-labeled) in female mice pretreated with Moloney leukemogenic virus (MLV) or a Rauscher pseudotype murine sarcoma virus [MSV(RLV)], Rauscher leukemogenic virus (RLV), or irradiated XM-1 tumor cells was studied by determining the ⁵¹chromium label in the spleens. Treatment of mice with MSV(MLV), or irradiated XM-1 tumor cells prior to challenge with the ⁵¹chromium-labeled tumor cells decreased the radioactivity in the spleen to 67-74% of the nonimmunized control value, while RLV or MSV(RLV) pretreatment did not alter the radioactivity retention. The decreased retention of radioactivity by the spleen paralleled the resistance to tumor cell transplantation suggests this method as an *in vivo* rapid screening technique.

- 0636 CONTROL OF MULTIPLICATION OF UNINFECTED MOUSE EMBRYO FIBROBLASTS AND MOUSE EMBRYO FIBROBLASTS CONVERTED BY INFECTION WITH MURINE SARCOMA VIRUS (HARVEY). (E.) Kotler, M. (Hadasa Sch. Hebrew U. Jerusalem, Israel). *Cancer Res* 30(10):2493-2496, 1970.

Cultures of mouse embryo fibroblasts were infected with murine sarcoma virus (MSV, 5 X 10⁵ focus forming units/ml cells) in order to observe the effect on cell multiplication of virus infection. Cells were treated with calf serum in amounts of 0 or 2% in a modified Eagle's medium. Starting 3 days after infection, the medium was changed daily and every second day some cells were harvested, and the relative population densities were determined. The uninfected cells multiplied to a limited extent in medium containing 0 or 0.5% serum. However, in medium containing 2%, the uninfected and MSV-infected cells multiplied at the same rate, and in medium containing 0.5% calf serum, the murine sarcoma-infected cells multiplied at a higher rate than the uninfected fibroblasts. Apparently, the cells formed by MSV produced some factor or factors which inhibits cell multiplication.

- 0637 MOLONEY STRAIN MURINE SARCOMA VIRUS (MSV-M)-INDUCED TRANSPLANTABLE OSTEOGENIC SARCOMA IN OSBORNE/MENDEL RATS. (It.) Ribbaudi, P. (Dept. Res. Cancer, U. Perugia, Italy). *Laboratory Pathology* 30(2):101-112, 1970.

Inoculation of Moloney Leukemia virus (MLV) at birth) to homozygous Osborne/Mendel rats followed by intracerebral inoculation of murine sarcoma virus (MSV-M), 10 days later, induced spinal osteosarcomas with pulmonary metastases as

the autopsy of a 273 day-old rat. The presence of large amounts of giant polynuclear cells at the peripheral regions of the neoplasm seemed to indicate the transformation effects of the viral agents inhibited on osteoclasts. Cell fragments of such neoplasms exhibited rapid growth *in vitro* with the formation of multilayer foci within 3-4 days after passage. Intraperitoneal inoculation of sarcomatous cells to 4-14 day-old syngeneic rats led to the rapid development of tumors and death within 2 months after inoculation. Acellular extracts from tumor tissue cultures and sarcomatous fragments from the first generation of transplants, inoculated into newborn BALB/c mice, produced no tumors 95 days after inoculation.

8 NONPRODUCER CLONES OF MURINE SARCOMA VIRUS TRANSFORMED BALB/3T3 CELLS. (E.)

Johnson, S. A. (Natl. Cancer Inst., Natl. Inst. Health, Bethesda, Md.) and W. P. Rowe. *Virology* 42(1):9-19, 1970.

Cultures of mouse embryo cells (BALB/c) were inoculated with murine sarcoma virus (2×10^5 virus-containing cells/culture dish), and 5 days later cultures were assayed for murine sarcoma virus. One of 20 foci selected at limiting dilution of murine sarcoma virus solution, 18 released both murine sarcoma virus and murine leukemia virus. Two focus-derived lines, however, showed no physical or biological evidence of virus production and contained evidence of antigens of the murine sarcoma-leukemia complex. These lines had altered properties in tissue culture and *in vivo* and were morphologically indistinguishable from virus-releasing murine sarcoma virus-transformed mouse lines. The addition of helper murine leukemia virus resulted in the rescue of the murine sarcoma virus genome from the host range and neutralization characteristics of the murine leukemia virus used to rescue. These findings indicate that virus production and release is not necessary for the maintenance of the transformed state in mouse cells and may suggest that murine sarcoma virus is capable of initiating transformation without murine leukemia virus. The sarcoma genome could be passed from parent to daughter cell for more than 100 generations in the nonproducer lines, in the absence of any detectable virus expression.

9 INHIBITION OF ONCOGENICITY OF MURINE SARCOMA VIRUS (HARVEY) IN MICE BY INTERFERON. (E.)

Man, L. D. (Boston City Hosp., Mass.). *Nature* 228(5265):1349-1350, 1970.

2-week old mice received i.p. injections of 0.1 ml of Harvey strain murine sarcoma virus, and, in some cases, a subsequent course of interferon injections (2 ml for 30 days), to test the effect of interferon administration on tumorigenesis. Interferon treatment produced a marked delay in mortality, with treated mice surviving for 20 wk postinfection (controls not treated with interferon died within 7 days

after infection with the virus.) Autopsy of treated and untreated mice revealed the erythroblastic splenomegaly and discrete peritoneal sarcomata characteristic of disease produced by Harvey murine sarcoma virus.

0640 THE REPRODUCTIVE AND CELL-TRANSFORMING CAPACITIES OF AVIAN SARCOMA VIRUS B77: INACTIVATION WITH UV LIGHT. (E.) Toyoshima, K. (Res. Inst. Microbial Dis., U. Osaka, Japan), R. R. Friis and P. K. Vogt. *Virology* 42(1):163-170, 1970.

A strain of avian sarcoma virus (Bratislava 77) was isolated from a virus-producing rat cell line subjected to UV irradiation to investigate the ability of UV-irradiated viruses to reproduce and to transform cells. Following UV-irradiation, 2 classes of radiation-damaged survivor virus particles were detected. The ability to release free virus from foci formed by UV-irradiated survivors was also impaired even in the presence of an avian leukosis virus helper. During 5-8 transfers of foci from these survivors a gradual disappearance of transformed cells from the culture was observed, indicating that there may have been a reversion to normal cell morphology due to death of transformed cells. The second class of particles could not transform cells, but produced pseudotypes with a strain of Rous sarcoma virus, interfered with avian sarcoma viruses of subgroup C, and was antigenically identical to the original strain of irradiated virus.

0641 LIGHT INACTIVATION OF FOCUS FORMATION BY CHICKEN EMBRYO FIBROBLASTS INFECTED WITH AVIAN SARCOMA VIRUS IN THE PRESENCE OF 5-BROMODEOXYURIDINE. (E.) Boettiger, D. (McArdle Lab., U. Wisconsin, Madison) and H. M. Temin. *Nature* 228(5272):622-624, 1970.

The effect of visible light on focus formation by chicken embryo fibroblasts (stationary cultures) infected with avian sarcoma virus (B77 or Schmidt-Ruppin) in the presence of 5-bromodeoxyuridine (5BUdR, 2-500 $\mu\text{g}/\text{ml}$) was studied after replating on a feeder layer of rat cells (resistant to infection). Cells infected with 8×10^4 focus forming units (f.f.u.)/cell and exposed to visible light (30 min) in the presence of 5BUdR exhibited an inactivation of focus formation to 5% of the control level (^3H -5BUdR studies showed that only 1% of the incorporated 5BUdR was associated with RNA, suggesting that sensitization to this reagent is a direct result of DNA incorporation). Autoradiographic and cell counting studies showed that the inactivation of focus formation was not a result of cell death or differences in plating efficiencies; focus production in cells infected at 3 f.f.u./cell was more resistant to the inactivation by light (31% survival of foci) than in cells infected at 0.15 f.f.u./cell (6% survival), suggesting that the new DNA is transcribed from viral genes (the increase in viral genes increased the number of copies of the new DNA which increased the resistance to light inactivation).

- 0642 THE INDUCTION OF TUMORS WITH ROUS SARCOMA VIRUS IN MICROTUS AGRESTIS: A PRELIMINARY NOTE. (E.) Smith, C. A. (Imp. Cancer Res. Fund., London, England) and R. J. C. Harris. *Arch Geschwulstforsch* 35(4):299-307, 1970.

Rous sarcoma virus in a 50% mince prepared from chick sarcoma was inoculated s.c. in amounts of 10^5 plaque-forming units in newborn field voles, and induction of tumors was observed after 8 months. Tumor induction appeared to be dependent on the amount of inoculum received, with 51 sarcomas induced in voles receiving 0.05 ml of inoculum, and 64 sarcomas induced in voles receiving 0.1 ml of inoculum. Half of the 41% of the animals which did not develop progressively growing tumors initially developed palpable tumors which then regressed. Cell-free virus rarely induced sarcomata. Seven tumors tested were not virus-producing but 2 of these were virogenic when passaged in association with chick cells. The sarcomas grew poorly in tissue culture and not at all as primary culture in soft-agar, but embryo fibroblast grew well *in vitro*.

- 0643 ROUS SARCOMA VIRUS-INDUCED CHANGES IN URIDINE AND UMP METABOLISM IN CHICK CHORIOALLANTOIC MEMBRANE. (E.) Dodge, W. H. (U. Mississippi Med. Ctr., Jackson), P. A. Morse, Jr. and G. A. Gentry. *Biochim Biophys Acta* 217(1):199-201, 1970.

A strain of Rous sarcoma virus (Fujinami) was inoculated into chick chorioallantoic membrane (10^4 tumor forming units/membrane specimen), and the uridine and/or UMP kinase reactions were investigated 7 days postinfection in the tissue homogenate supernatant. Uridine and UMP kinase were increased in virus infected tissue; a 36-fold increase in phosphorylation rate with the infected supernatant was noted when uridine was the reaction substrate and a 10-fold increase in the infected supernatant when UMP was the reaction substrate. Assay of UMP phosphatase activity revealed no significant difference between the normal supernatant and the infected supernatant fractions, but a 3-fold increase of uridine phosphorylase was found. The increased phosphorylation of uridine and UMP obtained with the infected supernatant fraction appears to be due to increased UMP kinase and uridine kinase and not to a decreased activity of the catabolic enzymes.

- 0644 OVERGROWTH-STIMULATING ACTIVITY OF DISRUPTED CHICK EMBRYO CELLS AND CELLS INFECTED WITH ROUS SARCOMA VIRUS. (E.) Rubin, H. (Dept. Molec. Biol., U. California, Berkeley). *Proc Nat Acad Sci* 67(3):1256-1263, 1970.

The ability of sonically disrupted embryo cells and cells which had been infected with Rous sarcoma virus to stimulate growth of cultured cells was investigated. Sparse (3×10^5 cells/60 mm dish) and dense (3×10^6 cells/60 mm dish) cultures of chick embryo cells were exposed to sonicates of cells from normal crowded cultures or of cells infected

with Rous sarcoma virus. Sonically disrupted cells caused a 6-fold rise in DNA synthesis and cell multiplication (as measured by ^3H -methylthymidine incorporation) when added to the medium of population density-inhibited cultures, but had little effect on the growth rate of sparse cultures. Sonicates from density-inhibited chick embryo cultures had much overgrowth-stimulating activity as did sonicates from actively growing cells. Sonicates of cells infected with Rous sarcoma virus showed a 10-fold increase in overgrowth-stimulating activity 3 days after infection. The activity in Rous sarcoma sonicates returned to near normal amounts at 7 days (^3H -methylthymidine cpm of 9550 and 11,400 for uninfected and infected cells, resp.) concurrently with the appearance of a high content of overgrowth-stimulating activity in the medium. The active overgrowth-stimulating material is nondialyzable. Apparently, rapid growth can be stimulated in density-inhibited cells by the release of some latent overgrowth-stimulating material which is released by sonication.

- 0645 SYNTHESIS OF RNA IN NORMAL AND ROUS SARCOMA VIRUS-INFECTED CELLS: EFFECT OF BROMODEOXYURIDINE. (E.) Levinson, W. E. (U. California Med. Ctr., San Francisco), J. M. Bishop, N. Quintrell, J. Jackson and L. Fanshier. *Virology* 42(1):221-224, 1970.

Gel electrophoresis was employed to examine RNA synthesis in normal and Rous sarcoma virus-infected chick embryo fibroblast tissue cultures which had been treated with bromodeoxyuridine in an attempt to inhibit host RNA synthesis while permitting viral RNA synthesis to proceed unaffected. While the rate of RNA synthesis in virus-infected cells was not affected by exposure to bromodeoxyuridine, normal cell RNA synthesis was reduced by 75% after a 48 hr exposure. Apparently, resistance to bromodeoxyuridine was induced specifically by Rous sarcoma virus. No change in virus replication was observed to follow bromodeoxyuridine treatment; the compound was added to cells 18 hr after infection; when bromodeoxyuridine was added 12 hr after infection, however, the yield of virus was reduced by a factor of 5. Neither infection of cells with Rous sarcoma virus, nor treatment with bromodeoxyuridine had a detectable effect on the rate of cellular RNA synthesis.

- 0646 THE LOW MOLECULAR WEIGHT RNAs OF ROUS SARCOMA VIRUS: I. THE 4 S RNA. (E.) Bishop, J. M. (U. California Sch. Med., San Francisco), W. E. Levinson, N. Quintrell, D. Sullivan, L. Fanshier and J. Jackson. *Virology* 42(1):182-195, 1970.

RNA extracted from purified Rous sarcoma virus was subjected to chromatography on methylated kieselguhr, resulting in the isolation of 4 categories of intravirion RNA including a large component of 4 S RNA, a discrete 7 S component, small quantities of 18 and 28 S RNA, and the 70 S RNA viral genome. The 4 S RNAs of the virus and host cell had identical electrophoretic mobility.

n 10% polyacrylamide gels and were methylated to the same extent. However, significant differences in nucleotide compositions were detectable. The virus apparently did not contain RNA corresponding to any of the other low molecular weight species of cellular RNA. The data were in accord with previous suggestions that RNA tumor viruses contain RNA acquired from the host cell during assembly; but they also suggested at least minor differences in composition between the cellular and viral 4 S RNA populations. That the viral 4 S RNA is not simply a contaminant derived from cellular debris is one conclusion prompted by reconstruction experiment results.

0647 A DNA-DEPENDENT DNA POLYMERASE AND A DNA ENDONUCLEASE IN VIRIONS OF ROUS SARCOMA VIRUS. (E.) Mizutani, S. (McArdle Lab., U. Wisconsin, Madison), D. Boettger and H. M. Temin. *Nature* 228(5270):424-427, 1970.

DNA-dependent DNA polymerase and a DNA endonuclease were identified in Schmidt-Ruppin Rous sarcoma virus by sucrose, cesium chloride, and cesium sulfate gradient analyses. A pronase digested reaction mixture (from a standard polymerase assay) produced a broad peak of 5-16 S material on a sucrose gradient, a peak with a density (g cm^{-3}) of 1.71 on a cesium chloride gradient, and a peak with a density of 1.42 on a cesium sulfate gradient, indicating that the product of the polymerase reaction was short double-stranded DNA (present as early as 1 min after the start of the reaction). Poly dA:dT was more effective as template (5.4-5.95 moles of labeled substrate incorporated) than poly T (0.45-0.47), poly dA (4.3-4.9), or poly rA:dT (0.4-1.85), suggesting that the enzyme preferred an ordered DNA-like structure as template; the better activity (pmoles ^3H -dTTP incorporated) with native *Escherichia coli* or calf thymus DNA (32.2 and 23, resp.) compared to the corresponding denatured DNA (20.2 and 13.2, resp.) confirms that double-stranded template was preferred. Incubation of the whole virion with labeled T7 DNA and subsequent analysis of the T7 DNA on a sucrose gradient revealed the presence of an endonuclease and suggested the possibility of a ligase system in the virion.

0648 DNA POLYMERASES OF ROUS SARCOMA VIRUS: DELINEATION OF TWO REACTIONS WITH ACTINOMYCIN. (E.) McDonnell, J. P. (Dept. Microbiol., U. California, San Francisco), A. C. Garapin, W. E. Levinson, N. Quintrell, L. Fanshier and J. M. Bishop. *Nature* 228(5270):433-435, 1970.

The response of polymerase from Rous sarcoma virus to actinomycin D was used to determine the presence of RNA-dependent and DNA-dependent DNA polymerases. High concentrations of actinomycin D (50 $\mu\text{g/ml}$) inhibited polymerase activity by 55%, and pretreatment of the polymerase mixture with ribonuclease produced a 66% inhibition; the residual DNA synthesis unaffected by actinomycin suggested that polymerase was able to use fragmented RNA as template. Equilibrium density gradients indicated that 2 classes of DNA resulted from

the polymerase reaction: one band was a complex between nascent DNA and viral RNA and was unaffected by the antibiotic; the second was a double-stranded DNA and was inhibited by actinomycin. Repeated sucrose density gradient centrifugations have demonstrated that the actinomycin-sensitive component was an integral part of the virion-associated polymerase and not merely an artifact.

0649 A MUTANT OF ROUS SARCOMA VIRUS (TYPE O) CAUSING FUSIFORM CELL TRANSFORMATION. (E.) Yoshii, S. (Nagoya U. Sch. Med., Japan) and P. K. Vogt. *Proc Soc Exp Biol Med* 135(2):297-301, 1970.

Chick embryo fibroblasts were infected with a virus derived from Rous associated virus which produced some foci with fusiform cell morphology, and this fusiform-transforming virus was subsequently isolated. The fusiform-transforming virus had the envelope properties of a strain of Rous sarcoma virus which causes round cell transformation and had an identical host range producing infections in chicken cells, in Japanese quail cells, and in pheasant cells. Three serum antigens which neutralize the infectivity of the round cell-transforming Rous sarcoma virus also neutralized the infectivity of the fusiform-transforming virus strain at the same titers required for round cell-transforming virus neutralization. Apparently, the fusiform-transforming and round-cell transforming viruses are mutants of the same virus.

0650 ROUS SARCOMA RECURRENCE AND ROUS SARCOMA VIRUS GROWTH IN CHICKEN MUSCLE. (E.) Dinowitz, M. (U. Arizona Sch. Med., Tucson) and H. Rabin. *Int J Cancer* 6(2):160-171, 1970.

Chickens which had been infected with Rous sarcoma virus (RSV), and in which the ensuing tumors had regressed, were re-inoculated with Rous-associated virus at the point of tumor regression (10^5 focus-forming units inoculated) to investigate the mechanism of tumor recurrence. Tumors recurred in one-third of those chickens that received 3 bi-weekly Rous-associated virus injections and in 1 chicken that received only a single Rous-associated virus injection. The tumors re-appeared from 6 to 19 wk after regression of the original tumors and within 4 wk of the last Rous-associated virus challenge. RSV was recovered from cultures of a recurring tumor as well as from a wing that developed subcutaneous blistering following Rous-associated virus inoculations. RSV was also obtained from 40% of "recovered" wing muscles explanted in tissue culture up to 3 months after regression. In addition, RSV was isolated from a tumor that recurred in one of 12 recovered chickens inoculated with Freund's adjuvant. In an attempt to determine if ageing of muscle contributed to resistance to infection and suppression of tumor recurrence, wings of 5-wk-old and 12-wk-old chickens were infected with RSV and Rous-associated virus, or Rous-associated virus alone. RSV and Rous-associated virus were recovered from most muscles explanted 48 hr or more after RSV infection of 5-wk-old chickens. However, when muscles from 12-wk-old

chickens were explanted 4 days after infection, little RSV was recovered, although most of the Rous-associated virus-infected wings produced Rous-associated virus in culture. This suggests that Rous-associated virus growth in older muscles is probably not the limiting factor in RSV growth. It is possible that RSV survived in the muscles of the immune chickens for a prolonged period after tumor regression, and that tumor recurrence was induced by inflammation and recruitment of new susceptible cells by the re-inoculated Rous-associated virus.

- 0651 COMPLEMENTARITY BETWEEN ROUS SARCOMA VIRUS (RSV) RNA AND THE *IN VITRO*-SYNTHESIZED DNA OF THE VIRUS ASSOCIATED DNA POLYMERASE. (E.) Duesberg, P. H. (Dept. Molec. Biol., U. California, Berkeley) and E. Canaani. *Virology* 42(3):783-788, 1970.

The complementarity between an *in vitro* synthesized ^3H -DNA of the Rous Sarcoma virus (RSV)-associated DNA polymerase and Schmidt-Ruppin (SR)-RSV RNA was determined by measuring the buoyant density in cesium sulfate before and after hybridization. ^3H -DNA hybridized with relatively large fragments of viral RNA, and after digestion with RNase the ^3H -DNA was resolved into 2 components with 60-70% at a density of 1.54 g/ml, indicating the amount of 60-70 S SR-RSV RNA hybridizable to ^3H -DNA (the 4 S component of SR-RSV RNA also contained RNA complementary to ^3H -DNA). At saturating concentrations of viral RNA, not more than 50-70% of the DNA hybridized to viral RNA to form DNA-RNA hybrids (the remaining DNA may have the same base sequence as the viral RNA or may have a completely different sequence), while with an excess of the viral RNA up to 75% of the RNA was transcribed to DNA.

- 0652 SARCOMA BLOCKADE *IN VIVO*: RABIES-ROUS SYSTEM IN CHICKENS. (E.) Desai, S. M. (Haffkine Inst., Bombay, India). *Nature* 228(5270):460-461, 1970.

The *in vivo* blockade of Rous sarcoma virus (RSV), determined by the absence of tumor for 21 days and the absence of plasma anti-RSV neutralizing antibody, by a vaccine strain of rabies virus (Semple vaccine) was studied in White Leghorn chickens. The chickens were highly susceptible to RSV (only 2% resistant), but rabies virus (titer of $10^{6.5}$ to $10^{7.2}$ for adult mouse $\text{LD}_{50}/0.03$ ml) given at the same time as RSV or 48 hr later increased the percentage of tumor-free chicks (22% and 44%, resp.) while rabies virus given 24 hr before RSV exhibited no blockade and given 24 hr after RSV exhibited a reduced effect (14%). Increasing the RSV dilution produced a graded increase in the percentage of tumor-free chicks, and the transient nature of the blockade became apparent when tumor-blocked chicks rechallenged with RSV after 30-49 days developed tumors. Anti-RSV neutralizing antibody was not found in tumor-blocked chicks suggesting that Rous associated viruses (RAV-4 and RAV-5) are also blocked.

- 0653 BRAIN TUMORS INDUCED WITH ROUS SARCOMA VIRUS, SCHMIDT-RUPPIN STRAIN: II. R TUMOR SPECIFIC TRANSPLANTATION ANTIGEN IN SUBCUTANEOUSLY PASSAGED MOUSE BRAIN TUMORS. (E.) Kumanishi, T. (Brain Res. Inst., Niigata U., Japan) and T. Yamamoto. *Jap J Exp Med* 40(2):79-86, 1970.

The existence of a Rous tumor specific transplantation antigen was shown in subcutaneously passaged brain tumors (2nd to 10th subcutaneous transplantation generations) which originally had been induced in adult mice with Rous chicken sarcoma cells produced by the Schmidt-Ruppin strain virus. All 4 of the passaged brain tumors studied (C3H-passaged early brain tumor, DDD-passaged early brain tumor, DDD-passaged delayed brain tumor, and CDF₁-passaged delayed brain tumor) exhibited the antigen; all cross-reacted with each other and with 2 lines of long-term passaged (more than 60 transplant generations) ascites sarcoma (SR-C3H/He and SR-DDC₁ ascites sarcoma) which originally had been induced in the subcutaneous region after neonatal inoculation of the same virus. In the immunized animals the tumors developed later, and the sizes of the tumors were always below the range observed in the control animals; the frequency of tumor take was also reduced, and the animals exhibited isograft resistance after 90-270 days of immunization. Mouse brain tumors apparently contain virus-induced tumor specific transplantation antigen which is common to all tumors produced by the same virus but not to chemically induced tumors (methylcholanthrene induced tumors could not be suppressed by simultaneous pretreatment with the Rous virus).

- 0654 FURTHER STUDIES ON TUMOUR-PRODUCING CAPABILITY IN ADULT MICE BY EMBRYONIC TISSUE CULTURES EXPOSED TO A VIRUS AND GRAFTED BEFORE ESTABLISHMENT OF MORPHOLOGIC TRANSFORMATION. (E.) Kryukova, I. N. (Acad. Med. Sci., Moscow, USSR), B. Obukh, T. I. Biryulina and O. V. Babkova. *Cancer* 6(2):275-282, 1970.

Rous sarcoma virus (Carr-Zilber strain) was used to infect embryonic tissue cultures derived from strains A, C3H-H2P, AKR, C57BL/Sn, CC57W, C127, B10.D2, and BALB/c and the infected cells were inoculated into syngeneic ($3-5 \times 10^6$ cells/mouse) to test the oncogenic properties of these cell implants. Mice of strains A, C3H-H2P, AKR, C57BL/Sn, and CC57W developed tumors with an incidence of 100% after latency periods of 4-12 wk. Only 2 of 10 CC57BR mice developed tumors, and no mice of strains B10.D2 or BALB/c developed tumors. However, infected cells originating from resistant mouse strains inoculated into F₁ hybrid mice produced crossing resistant and susceptible mouse strains caused tumors which consisted of cells of the resistant parental strain. Resistance to tumor induction of the 3 strains mentioned above was mediated by the strong immune reaction against the cells introduced. Tumor-production by infected untransformed cells was also seen with the Carr-Zilber strain in hamsters, with the Schmidt-Ruppin strain of Rous sarcoma virus in mice, and with

strain in hamsters but not in mice. No tumors are produced by inoculating mice with syngeneic embryonic tissue culture exposed to a neurotropic strain of influenza A viruses, or SV40.

0655 ANTIGENS OR ROUS VIRUS PARTICLES IN THE VIRUS-FREE TUMORS INDUCED IN ADULT RATS: FACTORS OF CELL AND HUMORAL IMMUNITY. (Rus.)

Uznetsova, N. N. (Acad. Med. Sci. USSR), V. Ya. Nevlyagin and T. I. Biryulina. *Biull Eksp Biol* 70(9):66-69, 1970.

Primary so called "virus-free" tumors, induced in adult Wistar rats by the Schmidt-Ruppin strain of Rous sarcoma virus, were examined for the presence of antigens to Rous virus particles. About 10% of rat Rous tumors had the antigens of virus particles, detected by the fluorescent antibody test. In 17% of the animals tested, the sera had group-specific antibodies detected by the complement fixation fluorescent test. Virus-neutralizing antibodies in the sera of rats were not discovered. About 50% of rats had the cellular immune activity against transplantation antigens of its own "virus-free" tumors. No humoral cytotoxic antibodies could be detected in the sera of rats with Rous tumors; nor was there any correlation of a cellular immune reaction with the presence of group-specific antibodies or antigens of virus particles in these tumors.

0656 CELLULAR IMMUNITY TO ROUS SARCOMA IN TUMOR-BEARING CHICKENS. (E.) Sjogren, H. O.

Dept. Med. Microbiol. Path., U. Lund, Sweden) and Jonsson. *Cancer Res* 30(9):2434-2437, 1970.

Thymus cells of Schmidt-Ruppin Rous virus (RSV-SR)-inoculated chickens bearing Rous sarcomas were tested *in vitro* for colony inhibition (method of Hellström) against the RSV-SR sarcoma cells. The thymus cells from 7 of the 8 RSV-SR inoculated chickens reduced colony formation of the plated Rous sarcoma cells by 20-48% when compared with thymocytes from untreated chickens (even thymocytes from the RSV-SR-treated chickens that had been stored frozen for 3 months maintained their inhibitory activity); thymus cells from the RSV-SR-treated chickens showed no colony inhibition in NIA control tumor, YAA-RC2 sarcoma, or A12B8 adenovirus type 12 tumor, demonstrating the specificity of the inhibitory effect.

0657 NUCLEIC ACID SYNTHESIS DURING THE FOCUS FORMATION BY SHOPE FIBROMA VIRUS ON GREEN MONKEY KIDNEY CELLS. (E.) Takehara, M. (Kobe Sch. Med., Japan). *Arch Ges Virusforsch* 31(3-4):303-312, 1970.

Focus formation and nucleic acid synthesis were studied in African green monkey kidney cells (AGMK) infected with Shope fibroma virus. The AGMK cell cultures were infected with 1-10 plaque-forming U of Shope fibroma virus, and infected and uninfected cultures were labeled with ^3H -thymidine (10 μC /culture bottle). Focus formation was observed as

localized piling up of cells at 3-5 days after viral infection. The number of foci increased in proportion to the size of the Shope fibroma virus inoculum 50 and 160 foci/culture bottle at 2 and 3 virus doses/culture, resp. In the Shope fibroma virus-AGMK cell system, however, the growth rate of virus was comparatively low and no apparent cytopathic effect was demonstrated as a result of virus infection. The incorporation of ^3H -thymidine into the nuclear fraction of infected cells was suppressed early in the cycle of virus replication (from 4 to 0.7 cpm/ μg DNA $\times 10^{-4}$ in 20 hr after virus infection) and before focus formation. On the other hand, the rate of DNA synthesis increased markedly in the infected cytoplasm (from 4 to 9.8 cpm/ μg DNA $\times 10^{-4}$ in 30 hr after viral infection). Accompanying the induction of viral DNA synthesis was a gradual increase in cytoplasmic RNA synthesis.

0658 *IN VITRO* CULTIVATION AND ANTIGENICITY OF COTTONTAIL RABBIT PAPILLOMA CELLS INDUCED BY THE SHOPE PAPILLOMA VIRUS. (E.) Ishimoto, A.

(Aichi Cancer Ctr., Nagoya, Japan), S. Oota, I. Kimura, T. Miyake and Y. Ito. *Cancer Res* 30(10):2598-2605, 1970.

Three cell lines of cottontail rabbit papilloma cells were cultured *in vitro* from cutaneous papillomas induced in rabbits by Shope papilloma virus, and another cell line was established from the skin of a normal rabbit; cytologic properties and antigenicity of these cultures were observed. All 4 cell lines consisted for the most part of spindle-shaped and polygonal cells. Cells from tumor tissue grew at a much faster rate than did cells of the normal rabbit skin, the cell counts on the 8th day of harvest for papillomatous and normal tissue being 340,000 and 110,000, resp. The viral antigen specific for Shope papilloma virus was demonstrated in the cytoplasm of cultured tumor cells by immunofluorescent staining. However, under electron microscopic observation, Shope papilloma virions were not detectable in the cytoplasm or nuclei. On the other hand, tumor-specific T-antigen and surface antigen were clearly demonstrated in the nuclei and on the cell membrane of the tumor cells, resp. These tumor cells were inoculated into domestic rabbits to examine whether the cells retain capacity to produce infectious Shope papilloma virus; no papillomatous growth or tumor development was observed at the site of inoculation in any of these rabbits.

0659 SUSCEPTIBILITY OF HUMAN CELL STRAINS TO TRANSFORMATION BY SIMIAN VIRUS 40 AND SIMIAN VIRUS 40 DEOXYRIBONUCLEIC ACID. (E.) Aaronson, S. A. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *J Virol* 6(4):470-475, 1970.

Early stages in simian virus (SV40) infection were examined to try to elucidate the step or steps responsible for the marked differences in susceptibility of human fibroblasts to transformation by SV40. Human fibroblast cell cultures from patients with genetic diseases, Fanconi's anemia, and Down's syndrome were exposed to SV40 and SV40 DNA. Tumor

antigen induction by SV40 and SV40 DNA was studied in transformation-susceptible, transformation-resistant, and normal cells, with the result that whole virus produced more tumor antigens in susceptible and normal cell types than did SV40 DNA (e.g., 22.0 and 2.1% of tumor antigen-containing cells were produced in susceptible and normal cells, resp., by SV40 DNA). However, in resistant cells SV40 DNA produced more tumor antigen-containing cells than did whole SV40 (e.g., 0.4 and 0.2% tumor antigen containing cells produced by SV40 DNA and SV40, resp.) The most transformation-susceptible cells infected with whole virus exhibited a level of transformation 1800 times in excess of the level exhibited by the most transformation-resistant cells; however, when cells were infected with SV40 DNA, susceptible and resistant cells showed no difference in transformation level. The elimination of the differences in transformation frequency with whole virus among cell strains by SV40 DNA suggests that the relative resistance of most cell strains to transformation is determined at an early step in infection.

- 0660 ANALYSIS OF SV40-INDUCED TRANSFORMATION OF HAMSTER KIDNEY TISSUE *IN VITRO*: VII. INDUCTION OF SV40 VIRUS FROM TRANSFORMED HAMSTER CELL CLONES BY VARIOUS AGENTS. (E.) Rothschild, H. (Harvard Med. Sch., Boston, Mass.) and P. H. Black. *Virology* 42(1):251-256, 1970.

Hamster kidney cell lines transformed by SV40 were exposed to various chemical and physical agents to investigate the yield of infectious virus induced from the hamster cell clones. One inducible line of cells (I_gAP1) was tested with the agents mitomycin C, acriflavine, 5-bromodeoxyuridine, caffeine and UV- and X-irradiation. Although all these agents except acriflavine were able to induce infectious virus from the cell clone, mitomycin C (2 µg/ml) induced the highest yield of virus. The dose of inducing agent and the amount of infectious virus produced were not always proportionally related. No combination of agents was more effective in inducing virus production than each agent used singly.

- 0661 SPECIFIC AGGREGATION OF SV40-TRANSFORMED CELLS BY ORNITHINE, LEUCINE COPOLYMERS. (E.) Duksin, D. (Weizmann Inst. Sci., Rehovot, Israel), E. Katchalski, and L. Sachs. *Proc Nat Acad Sci* 67(1):185-192, 1970.

A copolymer of L-ornithine and L-leucine was added to suspensions of a wide variety of normal and virally and nonvirally-transformed mammalian cells to investigate the agglutinating effect of this peptide on these cells. The basic copolymer studied rapidly agglutinated normal and transformed cells in the absence of serum, while in the presence of 10% calf serum, agglutination was inhibited. This copolymer and those of ornithine and valine and arginine and leucine produced, in the presence of serum, a specific aggregation of simian virus 40-transformed cells cultured for about 24 hr after addition of the peptide. The rapid agglutination and

SV40-specific aggregation could not be inhibited by a variety of individual amino acids or carbohydrates. The specific aggregation could be detected in suspensions of SV40-transformed and other cells, and was not prevented by X-irradiating the cells with 10⁵ r. Aggregation of the SV40-transformed cells was inhibited by acidic polyamino acids provided these were added not later than about 5 hr after addition of the basic copolymer. The results indicate that the basic copolymer, in the presence of serum, produces aggregation in SV40-transformed cells, presumably in the surface membrane, that causes the cells to aggregate. In addition to the aggregation of cells transformed by SV40, cells transformed by adenovirus 12, which do not contain detectable SV40-specific nuclear antigens, were also aggregated by the basic copolymer in the presence of serum. Apparently, SV40-induced changes in the surface membranes of cells transformed by adenovirus type 12 can be detected by the thine-leucine copolymer.

- 0662 THE EFFECT OF ACTINOMYCIN D ON DNA SYNTHESIS IN SV40 INFECTED EXPONENTIALLY GROWING AND STATIONARY CELLS. (Ger.) Fischer, H. (German Cancer Res. Ctr. Heidelberg, Germany). *K. Munk. Z Krebsforsch* 74(4):390-395, 1970.

The effect of actinomycin D (Ac-D) on DNA synthesis in SV40-infected *Cercopithecus* monkey renal cells was investigated by means of immunofluorescence, autoradiography in exponentially growing and stationary cell cultures. Inhibition of DNA synthesis was observed 25 hr after viral infection in the untreated exponentially growing cell cultures; then DNA synthesis resumed. A 30 min treatment with Ac-D (1 µg/ml) 2½-3 hr following SV40 infection of the renal cells led to a 10 hr inhibition of DNA synthesis followed by renewed synthetic processes; 30 hr after infection the number of labeled cells in the Ac-D-treated cultures was the same as that occurring at 45 hr after infection in the nontreated cultures. A decrease of DNA synthesis was noticed 10 hr after viral infection in untreated stationary cell cultures. Ac-D treatment 2½-3 hr after infection induced a further DNA synthesis 15 hr after infection, following a trend similar to that of untreated cells. The enhanced effects of Ac-D on the inhibition and renewal of DNA synthesis in the exponentially growing SV40-infected cells indicate a possible competition between the viral and cellular processes, as observed in the stationary cultures.

- 0663 ENHANCEMENT OF VIRAL TRANSFORMATION BY ULTRA-VIOLET LIGHT. (E.) Lytle, C. (Bureau Radiol. Hlth., Rockville, Md.), K. B. Hellman and N. C. Telles. *Int J Radiat Biol* 297-300, 1970.

The effect of UV irradiation in varying doses on cell susceptibility to transformation by SV40 was investigated. A line of mouse cells BALB/3T3 given UV irradiation in doses ranging from 13 to 130 erg/mm² of cell culture and then infected with virus. The colony-forming ability of the infected cells decreased with increasing UV dose. Total

colony-forming units after 136 erg/mm² UV numbered 1.3×10^5 ; after 544 ergs/mm², total colony-forming units numbered 1.0×10^3 . The appropriate figures for transformed colony units after 136 and 544 ergs/mm² UV were 4.4×10^3 and 1.6×10^2 , resp. Apparently, the fraction of surviving colonies which are transformed increases with UV dose. The UV target for transformation enhancement was apparently smaller than the target for inactivation of colony-forming ability for these cells. The findings seem to indicate that UV radiation is capable of enhancing viral tumorigenesis.

0664 EFFECT OF PROLONGED CULTIVATION OF SV40-TRANSFORMED MOUSE CELLS IN BROMODEOXYURIDINE OR PRETREATMENT WITH MITOMYCIN C ON RESCUE OF SV40. (E.) Dubbs, D. R. (Baylor Coll. Med., Houston, Tex.) and S. Kit. *Int J Cancer* 6(2):223-233, 1970.

The genetic effect of prolonged culturing of primary mouse kidney cells transformed by UV-irradiated SV40 (mKS-U cell lines) with 5-bromodeoxyuridine (10 µg/ml) and the effect of mitomycin C pretreatment (1 µg/ml for 20 hr) on rescue of SV40 were determined. Four of the cell lines grown with 5-bromodeoxyuridine became deficient in thymidine kinase activity [mKS-U3(BU), mKS-U5(BU), mKS-U13(BU), and mKS-U18(BU)] while mKS-U1(BU) and mKS-U2(BU) retained thymidine kinase activity. The thymidine kinase-deficient lines were unable to grow in a medium with hypoxanthine, aminopterin, thymidine, and glycine because of their inability to use the exogenous thymidine as a source of thymidylate when aminopterin blocked the *de novo* synthesis. The bouyant densities in cesium chloride of DNA from the thymidine kinase-deficient lines were normal (1.703 g cm^{-3}) compared to the heavier DNA isolated from the cell lines grown in 5-bromodeoxyuridine which maintained thymidine kinase activity (1.722 g cm^{-3}). The SV40 T antigen was maintained in all the cell lines even after prolonged cultivation with 5-bromodeoxyuridine. Rescue of SV40 from the mKS-U(BU) lines by fusion with CV-1 cells (African green monkey kidney cells) in the presence of UV-Sendai virus after serial passage in 5-bromodeoxyuridine was not altered in the average or good yielder transformed lines, although 2 poor yielders (mKS-U1 and mKS-U3) produced medium-sized and clear infectious plaques after 5-bromodeoxyuridine passage. No SV40 could be rescued from rare or non-yielder lines after serial passage. Pretreatment with mitomycin C before fusion with CV-1 cells did not affect the yield from the good yielder (mKS-U13) and did not permit SV40 rescue from rare or non-yielder lines.

0665 CHROMOSOMES OF SV40 TRANSFORMED HUMAN AMNION CELLS AFTER MYCOPLASMA INFECTION. (E.) Fogh, J. (Sloan-Kettering Inst. Cancer Res., New York, N.Y.), H. Fogh and M. Dowling. *Proc Soc Exp Biol Med* 135(2):206-211, 1970.

Primary cultures of human amnion cells were infected concurrently with SV40 and the HT strain of mycoplasma in order to investigate the modifications in chromosome numbers and the frequencies of chromosome

abnormalities related to the presence of mycoplasma in the virus-transformed cultures. Chromosome numbers in cells infected with SV40 had changed to the hypertriploid-hypotetraploid range when examined 145 days after infection; numbers in cells infected with both virus and mycoplasma generally remained in the diploid range up to 207 days post-infection at which time about 50% of cells were in the hypertriploid-hypotetraploid range. In the virus-infected group, there was a gradual reduction in the numbers of chromosomes after the 145th day post-infection, and chromosome abnormalities were generally more frequent than in cells infected with both virus and mycoplasma; the frequency of abnormalities increased with elapsed time post-infection. From 183-242 days post-infection, 96% of virus-infected cells showed di- and polycentric chromosomes, as compared to 77% of virus-and mycoplasma-infected cells. Acentric chromosome fragments occurred in 33 and 13%, resp., of virus-infected and virus- and mycoplasma-infected cells. Percentages of minute chromosomes in the 2 infection groups were 47 and 31%, resp. After mycoplasma elimination, chromosome numbers and aberrations were not reversed, but the occurrence of large telocentric chromosomes was more frequent.

0666 TEMPERATURE-SENSITIVE SIMIAN VIRUS 40 MUTANT DEFECTIVE IN A LATE FUNCTION. (E.)

Kit, S. (Baylor Coll. Med. Houston, Tex.), S. Tokuno, K. Nakajima, D. Trkula and D. R. Dubbs. *J Virol* 6(3):286-294, 1970.

A cell-line of monkey kidney cells was infected with a strain of SV40 (infection multiplicity of 5 plaque-forming units/cell in a 0.2 ml volume) and then treated with the mutagen nitrosoguanidine in doses of 100 µg/ml culture for the purpose of isolating a SV40 mutant which replicated at differing rates in differing temperature conditions. Replication of virus, designated tsTNG-1, at the nonpermissive temperature (38.7°C) was 3,000-fold less than at the permissive temperature (33.5°C). Plaque formation by the mutant strain's DNA on kidney cell culture monolayers occurred normally at 33.5°C but was grossly inhibited at 38.7°C. The time at which virus replication was blocked at 38.7°C was determined by temperature-shift experiments. In shift-up experiments, cultures infected for various times at 33.5°C were shifted to 38.7°C. In shift-down experiments, cultures infected for various times at 38.7°C were shifted to 33.5°C. All cultures were harvested at 96 hr postinfection. No virus growth occurred when the shift-up occurred before 40 hr postinfection. Maximum virus yields were obtained at 96 hr postinfection when the shift-down occurred at 66 hr, but only 15% of the maximum yield was obtained when the shift-down occurred at 76 postinfection. These results indicate that tsTNG-1 contains a conditional lethal mutation in a late viral gene function. The mutant synthesized tumor antigen, viral capsid antigens, and viral DNA, and induced thymidine kinase activity at either 33.5 or 38.7°C. The properties of the viral DNA synthesized in mutant-infected kidney cell culture cells at 33.5° or 38.7°C were very similar to those

of SV40 DNA made in parental virus-infected cells, as determined by nitrocellulose column chromatography, cesium-chloride-ethidium bromide equilibrium centrifugation, and by velocity centrifugation in neutral sucrose gradients. Mutant tsTNG-1 enhanced cellular DNA synthesis in primary cultures of mouse kidney cells at 33.5° and 38.7°C and also transformed mouse kidney cultures at 36.5°C. After fusion with susceptible monkey kidney cell cultures and incubation at 38.7°C, the mutant could not be recovered from a clonal line of transformed cells; however, after incubation at 33.5°C, recovery was possible.

- 0667 EFFECT OF LOSS OF THYMIDINE KINASE ACTIVITY ON THE TUMORIGENICITY OF CLONES OF SV40-TRANSFORMED HAMSTER CELLS. (E.) Rothschild, H. (Massachusetts Gen. Hosp., Boston) and P. H. Black. *Proc Nat Acad Sci* 67(2):1042-1049, 1970.

Characteristics of cells (derived from transplantable SV40-transformed hamster kidney cells) deficient in thymidine kinase (TK⁻) were studied. Wild type cells (TK⁺) incorporated 100 times as much ³H-thymidine (11.0-23.0 x 10³ cpm/10⁶ cells). TK⁺ cells had a large variation in chromosome number (53-114 chromosomes) while TK⁻ cells (T8 BU 1-1) had relatively constant modal numbers (52-54 chromosomes). Tumors initiated by TK⁺ cells appeared in 95% of the animals 2-8 wk after inoculation, while only 1 tumor was observed in hamsters inoculated with TK⁻ cells by the 8th wk. Cells harvested from tumors induced with TK⁻ cells and revertant cell lines (spontaneous or chemically mutated) obtained from TK⁻ cells showed thymidine kinase activity to be intermediate between that of the wild type and the enzyme-deficient cell lines. The thymidine kinase salvage pathway enzyme may play a rate-limiting role in tumorigenesis.

- 0668 EFFECT OF ULTRAVIOLET IRRADIATION ON THE SURVIVAL OF SIMIAN VIRUS 40 FUNCTIONS IN HUMAN AND MOUSE CELLS. (E.) Aaronson, S. A. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *J Virol* 6(4):393-399, 1970.

The effect of UV irradiation on viral functions, including transformation ability, tumor-antigen production, and virus-antigen production was investigated; mouse and human cells were exposed to SV40 which had received 24 ergs/mm² culture of UV at wavelengths of 253.7 nm for varying periods of time (5-20 min). Transformation appeared to be less UV-sensitive than either tumor- or virus-antigen when all functions were compared in the same cell. However, the time course of both tumor- and virus-antigen appearance was delayed with UV-irradiated virus, so that the survival curves of these functions changed with time. Mouse and human cells which were transformed by UV-SV40 all contained SV40 antigen. Infectious virus could be recovered from many more transformants than would be expected from the infectivity in African green monkey kidney cells of the irradiated virus. Apparently, UV-damaged SV40 can be reactivated by human and mouse cells.

- 0669 ANTIGENIC STUDY OF UNFERTILIZED MOUSE CROSS REACTIVITY WITH SV40-INDUCED ANTIGENS. (E.) Baranska, W. (Wistar Inst. Anat. Biol., Philadelphia, Pa.), P. Koldovsky and H. Koprowski. *Proc Nat Acad Sci* 67(1):193-199, 1970.

The antigenic properties of a mammalian ovum at earliest stage of development were studied by preparing an anti-egg serum from guinea pigs immunized with unfertilized eggs from virgin C57BL/6. This serum was introduced into preparations of eggs obtained from allogeneic and syngeneic mice, rat eggs, lymph node cells, methylcholanthrene-induced tumor cells, normal mouse embryo cells from syngeneic or allogeneic mice, and SV40-transformed mouse embryo cells. Cytotoxicity and immunofluorescence tests showed that the anti-egg serum was cytotoxic for eggs of mice syngeneic and allogeneic with the donors of the immunizing eggs but not cytotoxic for rat eggs, lymph node cells, methylcholanthrene-induced tumor cells, or normal mouse embryo cells. However, anti-egg serum was cytotoxic for SV40-transformed mouse embryo cells. This cross reactivity between the SV40-transformed cells and mouse eggs was further supported by the elimination of cytotoxicity of the anti-egg serum for mouse eggs after absorption with SV40 transformed cells. Viral transformation may have altered the structure of the embryo cell surface in such a way as to make it sensitive to the anti-egg serum.

- 0670 INDUCTION OF SV40 TRANSPLANTATION ANTIGEN (TrAg) DURING THE LYTIC CYCLE. (E.) Girardi, A. J. (Wistar Inst. Anat. Biol., Philadelphia, Pa.), and V. Defendi. *Virology* 46:688-698, 1970.

The induction of SV40 transplanted antigen (TrAg) in vaccinated hamsters and the inhibition of TrAg production by various agents was investigated. Hamsters were inoculated with a tumor-inducing dose of SV40 (0.2 ml) at birth, and were subsequently given a vaccination injection of SV40-infected African green monkey kidney cells (AGMK) in doses of 10^{7.2} plaque-forming units during the latent period of tumor-induction. The appearance of SV40 TrAg was blocked by (cycloheximide, 20 µg/ml), or by a level of actinomycin D (5 µg/ml) that inhibits early and late viral functions. Antigen induction was not blocked by inhibitors of DNA synthesis (fluorodeoxyuridine, 25 µg/ml) or by a level of actinomycin D (0.5 µg/ml) that ordinarily permits expression of early viral functions. When virus matured in the infected cells in the absence of chemical inhibitors, or after drug withdrawal, yield of infectious virus was not sufficiently high to account for the development of tumor resistance in the hamsters. The ability of infectious SV40 to induce tumor resistance in hamsters was related to the quantity of tumor-inducing virus given to born hamsters: animals given large amounts of virus at birth were refractory toward immunization by even high levels of infectious virus. However, SV40-infected AGMK cells effected immunization of these animals.

- 0671 QUANTITATIVE ASPECTS OF IMMUNIZATION AGAINST PRIMARY SV40-INDUCED TUMORS. (E.) Kaliev, J. (Acad. Med. Sci. USSR, Moscow). *Neoplasma* 17(4):373-376, 1970.

The interruption of SV40-induced carcinogenesis by immunization of infected animals with the same virus during the latent period was studied quantitatively. SV40 preparations were injected s.c. in newborn hamsters in amounts ranging from 1.7×10^6 - 1.7×10^7 tissue culture infectious dose (TCID) of virus; after 3 wk, 50% of hamsters were immunized by i.p. injection 1.2×10^8 TCID of SV40. In a related experiment, newborn hamsters were infected s.c. with 1.5×10^6 TCID of SV40, and subsequently immunized with varying amounts of the virus. Immunization during the latent period before tumor appearance after initial infection significantly inhibited tumor development, with animals receiving the higher infectious dose of virus developing a higher percentage of tumors than animals receiving lower doses of virus (tumor induction of 21% and 10% for high and low dose hamsters, resp.) Mean latent periods before tumor appearance were markedly longer in immunized hamsters than in nonimmunized controls (178 and 115 days for immunized and non-immunized hamsters receiving 1.7×10^7 TCID of virus, resp.) In the second experiment, hamsters receiving immunizing doses of virus developed tumors in 3.3% and 26.7% of cases when injected with 1.2×10^8 and 1.2×10^7 TCID of immunizing viruses, resp., and in 74.4% of cases when no immunizing dose of virus was administered.

- 0672 INVESTIGATIONS ON THE HISTOGENESIS OF LEUKOSIS INDUCED BY SYRIAN HAMSTER PAPOVA VIRUS. (Ger.) Fey, F. (German Acad. Sci., Berlin), T. Schramm, E. Bender and M. Rudolph. *Arch Geschwulstforsch* 36(1):10-18, 1970.

Following the inoculation of hamster papova virus, the induced leukoses of tumor type occur mainly in the liver and thymus. Leukoses with typical enlargement of the lymph nodes and leukotic tumors of the mesentery are less frequent. The histogenesis of leukosis induced by this virus was investigated in the newborn hamster by s.c. injections of 0.2 ml by means of histochemical enzyme reactions. The first pathological change following the inoculation occurred in 4 days showing an atrophy of the thymus, and this change was observed in all the experimental animals until the 18th day after inoculation. Histologically there was a gradual decrease of lymphocytes in the cortical area. Pyknotic lymphocytes and phagocytes were abundant, and the extremely atrophied thymus consisted almost exclusively of reticular cells. A direct virus action upon the livers of newborn hamsters may be related to the fact that as long as 5 days after birth there are areas in the liver of myeloid and erythrocyte formation. It is postulated that the leukocytic tumors become manifest in the vascular areas when infiltration sets in.

- 0673 BEHAVIOR OF TISSUE CULTURE CELLS INFECTED WITH POLYOMA VIRUS. (E.) Dulbecco, R. (Salk Inst. Biol. Stud., San Diego, Calif.). *Proc Nat Acad Sci* 67(3):1214-1220, 1970.

Induction of movement, cell survival, mitotic rates, growth parameters, and cell morphology of tissue culture cells (3T3 and BALB/c-3T3 lines) infected with the oncogenic polyoma virus or its temperature-sensitive mutant (Ts-a) were studied. In medium containing 0.15% horse serum the induction of movement across a wound (produced with a glass rod) occurred simultaneously with the induction of DNA synthesis. Infection with Ts-a protected the cells from death at suboptimal serum concentrations, but there was no difference in cell survival between polyoma virus- or mock-infected cultures. Mitosis decreased in mock-infected cells after 20 hr but persisted in Ts-a-infected cultures. The wound serum requirement and topoinhibition of the mock-infected cells were decreased in polyoma virus-infected and Ts-a-infected cells (60-90%). The flat, round-shaped cells of serum-starved 3T3 or BALB/c-3T3 cultures became thick and elongated after infection, similar to changes that occur in cell transformation.

- 0674 THE SYNTHESIS AND BREAKDOWN OF NUCLEIC ACIDS IN MAMMALIAN CELLS TRANSFORMED BY ONCOGENIC VIRUSES: I. PURIFICATION AND PROPERTIES OF AN ENDONUCLEASE FROM BABY HAMSTER KIDNEY CELLS TRANSFORMED BY POLYOMA VIRUS. (E.) Koh, J. K. (U. Maryland Sch. Med., Baltimore), A. Waddell and H. V. Aposhian. *J Biol Chem* 245(18):4698-4707, 1970.

An endonuclease from a continuous line of baby hamster kidney cells transformed by polyoma virus (BKH21 C13/PyH3) was purified 1000-fold (DEAE-cellulose, phosphocellulose, and hydroxylapatite column chromatography) and characterized. The enzyme (molecular weight of 76,000) hydrolyzed heat-denatured DNA, RNA, and homopolynucleotides; native DNA was not affected. The enzyme appears to prefer polynucleotides which lack ordered structures as substrates, and evidence suggests that the DNase and RNase reside in the same protein. The optimum pH was between 8.7 and 9.5, and Mg^{++} (0.4-0.8 mM) or Mn^{++} (0.04 mM) was required for enzyme activity, while sodium or potassium chloride (10 mM) inhibited the activity by approximately 50%. The products of the hydrolysis of polyadenylate or polydeoxythymidylate were 5'-phosphate-terminated oligonucleotides. A similar enzyme appears to be present in normal baby hamster kidney cells.

- 0675 TRANSFORMATION OF HUMAN CELLS BY POLYOMA AND ROUS SARCOMA VIRUSES MEDIATED BY INACTIVATED SENDAI VIRUS. (E.) Shevliaghyn, V. J. (Gama-leya Inst. Epidem. Microbiol., Moscow, USSR) and N. V. Karazas. *Int J Cancer* 6(2):234-244, 1970.

Transformation of embryonic human fibroblasts was accomplished by polyoma and Rous sarcoma viruses in

the presence of inactivated Sendai virus. Treatment of the human cells with inactivated Sendai virus (hemagglutination titer of 1:40,000) followed by polyoma virus produced a stable transformed cell line, P-2, and treatment with Rous sarcoma virus followed by the inactivated Sendai virus produced a stable transformed cell line, 23. Both transformed cell lines differed morphologically from normal cells and had karyological abnormalities (decreased numbers of chromosomes in groups A and B and increased numbers in group C as well as some marker chromosomes) but contained human chromosome sets. The cell lines P-2 and 23 were able to grow in suspension and produced tumors in the cheek pouches and brains of hamsters, and factors were found in the media of both cell lines that were capable of transforming mouse and human cells.

- 0676 POLYOMA "TUMOR ANTIGEN": AN ACTIVATOR OF CHROMOSOME REPLICATION? (E.) Weil, R. (Inst. Molec. Biol., U. Geneva, Switzerland) and J. Kara. *Proc Nat Acad Sci* 67(2):1011-1017, 1970.

The time and temperature relation between the appearance of T-antigen and the activation of the cellular DNA-synthesizing apparatus was studied by immunofluorescence in contact-inhibited mouse kidney tissue culture cells infected with polyoma virus. The events of the polyoma lytic cycle were essentially the same at 37 C and 27 C although they proceeded at a slower rate at the lower temperature. At 37 C T-antigen was detected in 80-100% of the infected cells after 16-20 hr, and the lag between the appearance of T-antigen and the onset of polyoma-induced DNA synthesis varied from 2-8 hr. At 27 C T-antigen was detected after 50-60 hr, and the lag between the appearance of T-antigen and the onset of DNA synthesis varied from 15-20 hr to more than 3 days. Polyoma-infected cultures incubated at 27 C and transferred to 37 C for a 1 hr incubation before the onset of polyoma-induced DNA synthesis had no more DNA-synthesizing cells than mock-infected cells: when infected cells were transferred to 37 C for more than 3 hr the numbers of DNA-synthesizing cells increased with time. When these cells were transferred to 37 C after the onset of polyoma-induced DNA synthesis, the number of DNA-synthesizing cells increased by a factor of 1.5-2. The early period (time between the adsorption of polyoma virus and the appearance of T-antigen) was increased from 12 hr at 37 C to 30 hr at 27 C, and infected cells incubated at 37 C for 12 hr before transfer to 27 C exhibited polyoma-induced synthesis within 30 hr after infection. However, the kinetics of the increase in DNA-synthesizing cells was similar to cells that had been kept at 27 C throughout suggesting that a "psychrosensitive (time and temperature dependent) event(s) begins only after the early period.

- 0677 POLYOMA VIRUS-TRANSFORMED CELLS; THEIR AGING AND VIRUS GENERATION *IN VITRO*. (It.) Pitzurra, M. (Inst. Microbiol. Hyg., U. Perugia, Italy) and F. Bistoni. *Boll Soc Ital Biol Sper* 46(5):215-218, 1970.

Culture media of a B-line of polyoma virus-transformed cells (69th passage, B69,) consisting of Medium 199 and 10% calf serum were used after 33 days of incubation to test the capability of transformed cells to generate viruses. The medium was added to primary cultures of mouse embryo tissues (0.2 ml of B69) and inoculated into 14 day-old hamsters (0.2 ml B69 i.p. to 8 animals which were sacrificed 62 days later). Control hemagglutination activity was determined with immune anti-polyoma serum obtained from adult male hamsters which were inoculated at birth with 0.4 ml of polyoma virus stock suspension containing 10^8 oncogenic U/ml twice at 20 day intervals and a pool of serum with a hemagglutination titer of 1/12,800 in 0.2 ml was obtained 10 days after the second inoculation. Cytopathic effects occurred 9 days after infection in embryo cultures, and hemagglutination activity appeared in the culture medium supernatant 8 days after B69 inoculation; both effects were transmissible in the culture medium supernatant to similar primary tissue cultures. Tumors occurred in 6 of 8 hamsters 2 months after inoculation. Hemagglutination activity of B69 was completely inhibited by hamster antipolyoma immune serum. B-line cells that were transformed by virus polyoma *in vivo* are apparently able to produce hemagglutinative and infective virus after 30 days of *in vitro* cultivation.

- 0678 INTERFERON-SENSITIVITY OF THE ENHANCED INCORPORATION OF THYMIDINE INTO CELLULAR DNA INDUCED BY POLYOMA VIRUS. (E.) Dulbecco, R. (Salk Inst. Biol. Stud., San Diego, Calif.) and Johnson. *Virology* 42(2):368-374, 1970.

The effect of large doses (100 and 200 U/ml) of purified interferon (produced in L-929 cells with Newcastle Disease virus) on the induction of cellular and viral DNA synthesis by polyoma virus and its Ts-a mutant in 3T3 cells was studied. Interferon (100 U/ml) inhibited ^3H -thymidine incorporation into both viral (64-73% inhibition) and cellular (40-75%) DNA in polyoma-infected cells to similar extent; as it also inhibited label incorporation into cellular (56-62%) DNA in Ts-a-infected cells. ^3H -Thymidine incorporation was also slightly inhibited by interferon in uninfected cells (13%) but this was probably caused by the high doses of interferon used and by its high degree of purity.

- 0679 RESTORATION OF NORMAL GROWTH BY COVERING OF AGGLUTININ SITES ON TUMOR CELL SURFACES. (E.) Burger, M. M. (Dept. Biol. Sci., Princeton U., N. J.) and K. D. Noonan. *Nature* 228(5271):515, 1970.

The efficacy of covering agglutinin sites on virus-transformed cells for restoring normal growth-inhibition patterns to those cells was investigated. Polyoma virus-induced tumor cells (Py3T3) were incubated with trypsinized concanavalin A, and agglutination assays were performed. Preincubation with trypsinized concanavalin A radically increased the amount of agglutinin necessary to bring about

agglutination of cells, with untreated transformed cells requiring 250 µg/ml agglutinin, and normal and concanavalin A-treated cells requiring less than 1500 µg/ml agglutinin. The higher the density of cells in culture treated with concanavalin A, the earlier the onset of growth inhibition occurred, suggesting that the inhibiting effect of concanavalin A covering induced a genuine contact-inhibition effect, rather than a simple prevention of cell growth *per se*. Apparently it is the absence of the layer covering the agglutination site, and not the exposure of the agglutinin receptor layer, which accounts for the loss of contact inhibition of growth in virally-transformed cells.

0 ABSENCE OF A CELL MEMBRANE ALTERATION FUNCTION IN NON-TRANSFORMING MUTANTS OF POLYOMA VIRUS. (E.) Benjamin, T. L. (Publ. Hlth. Res. Inst. New York, N.Y.) and M. M. Burger. *Proc Nat Acad Sci* 67(2):929-934, 1970.

The ability of polyoma virus infection to expose an agglutinin-binding site on the membrane of cells was investigated. Normal mouse cells cultured with or without germ agglutinin were infected with polyoma virus (5-10 plaque-forming units/cell), and the agglutination was observed. Although oncogenic viruses expose the agglutination site on the cell membranes, non-transforming polyoma virus mutants do not (infection of normal mouse cells with these mutants produced 0% agglutination). In transforming wild-type polyoma virus infection, however, did expose the agglutination-site, producing 10-15% agglutination. Inhibitors of DNA synthesis, such as thymidine and 5-fluorodeoxyuride-5'-P, blocked the exposure of the agglutinin-binding site by wild type polyoma virus, but this blockage was reversed when conditions allowing DNA synthesis were restored. The findings suggest that the agglutinable state of the cell membrane is important in the loss of regulation of cell growth associated with carcinogenesis.

1 HOST RANGE MUTANTS OF POLYOMA VIRUS. (E.) Benjamin, T. L. (Publ. Hlth. Res. Inst., New York, N.Y.). *Proc Nat Acad Sci* 67(1):394-399, 1970.

The 3T3 line of Swiss mouse embryo fibroblast was used as the normal line from which a line of polyoma-transformed virus-free cells was isolated which was fully susceptible to lytic infection by polyoma virus. This line was used to select virus mutants which had lost most or all of their ability to grow like the untransformed parental line while retaining the ability to grow in the transformed derivative; mutagens used were hydroxylamine (incubation of cells with 0.4M soln at pH 7.0 at 45° for 90 min) and N-methyl-N'-nitro-N-nitrosoguanidine (314 µg/ml for 33 hr starting at the 17th hr of infection). The virus mutants with the desired properties were isolated (NG-18, NG-23, HA-33 and NG59). These virus mutants were also defective in their ability to transform cells of rat or hamster origin. The cell extracts from the mutants had the same host

range as the whole virus, indicating that the mutants were blocked at some intracellular step which is necessary both for transformation in rat or hamster cells, and for the completion of virus development in mouse cells.

0682 ENHANCED ONCOGENESIS ASSOCIATED WITH LYMPHOID CELL LYSIS FROM VIRUS INFECTION AND ANTITHYMOCYTE SERA TREATMENTS. (E.) Minton, J. P. (Dept. Surg., Ohio St. U., Columbus), M. C. Dodd, M. M. Al-falluji, and M. Allietta. *Curr Topics Surg Res* 2:239-246, 1970.

The effects of antithymocyte serum on oncogenesis induced in mouse spleens by polyoma virus was investigated. Newborn mice (DBA/2J) were given injections of 2×10^5 TCID₅₀/0.5 ml polyoma virus, with or without associated i.p. injections of antithymocyte serum (ATS) (0.1 ml). Mice from all experimental groups were killed and their spleens were prepared for light and electron microscopic examination. Of 81 mice receiving ATS and virus, all but 14 died, and all of the 14 survivors developed tumors by 6 months postinfection. Mice which received ATS and virus early in life developed tumors sooner than mice treated later in life. None of the mice receiving ATS alone, virus alone, rabbit serum, or no treatment showed enhanced tumor development. On splenic examination, mice which had received 4 or more ATS injections had markedly enlarged spleens (spleen wt 600 mg average) compared to normal mice (180 mg), and mice receiving virus had depressed spleen wt (110 mg). After 4 injections of ATS, lymphoid follicles had lost their normal morphological pattern and presented the appearance of diffuse masses of transformed "blastoid" cells. These cells showed a marked increase in cytoplasm and in polyribosome formations. The ATS treatments may have been responsible for the blastoid transformation of splenic lymphoid cells; the loss of immune competence brought about by the ATS may have permitted the enhanced growth of tumors.

0683 DNA AND GENE THERAPY: UNCOATING OF POLYOMA PSEUDOVIRUS IN MOUSE EMBRYO CELLS. (E.) Osterman, J. V. (U. Maryland Sch. Med., Baltimore), A. Waddell and H. V. Aposhian. *Proc Nat Acad Sci* 67(1):37-40, 1970.

Mouse embryo cell cultures were infected with polyoma virus, with the result that pseudovirions and polyoma virions were produced. The polyoma pseudovirions consisted of host DNA fragments encapsidated by polyoma virus-coat protein; they were adsorbed and uncoated by the mouse embryo cells. Ninety min after infection, 75% of the virions had been adsorbed and 6% of the adsorbed virions were uncoated. Pancreatic DNase converted the uncoated pseudovirus DNA from an acid-insoluble to an acid-soluble form, indicating that the pseudovirus had been uncoated. The cellular site of pseudovirus uncoating is unknown.

- 0684 RAPID CONCENTRATION AND PURIFICATION OF POLYOMA VIRUS AND SV40 WITH POLYETHYLENE GLYCOL. (E.) Friedmann, T. (Salk Inst. Biol. Stud., San Diego, Calif.) and M. Haas. *Virology* 42(1):248-250, 1970.

Baby mouse kidney cells were infected with polyoma virus (large plaque variants) at an input multiplicity of 10 plaque-forming units/cell, and confluent BSC-1 cells were infected with SV40 at an input multiplicity of 2 plaque-forming units/cell. The infected cells were precipitated with polyethylene glycol in a single-phase precipitation; the virus pellets were further purified by band sedimentation in CsCl. Both viruses were recovered quantitatively and retained infectivity. Results showed that the oncogenic polyoma and SV40 viruses can be concentrated and purified rapidly by polyethylene glycol precipitation, and that such a recovery method may be more effective than methods previously employed.

- 0685 INHIBITION OF POLYOMA-VIRUS ONCOGENESIS IN RATS BY POLYRIBOINOSINIC-RIBOCYTIDYLIC ACID. (E.) Vandeputte, M. (Rega Inst., U. Leuven, Belgium), S. K. Datta, A. Billiau and P. De Somer. *Europ J Cancer* 6(4):323-327, 1970.

Rats were inoculated with polyoma virus in association with an i.p. injection of polyriboinosinic-polyribocytidylic acid to investigate the inhibition of tumorigenesis by this compound. Polyriboinosinic-polyribocytidylic acid (100-300 µg dose, total of 0.96-1.36 mg) significantly reduced the incidence of tumors in virus-infected rats (62-72%) compared to controls (91%); this protective effect was observed not only when polyriboinosinic-polyribocytidylic acid was given before and immediately after the virus inoculation also when polyriboinosinic-polyribocytidylic acid treatment was started 7-21 days after inoculation. This finding indicates that mechanisms other than an interferon antiviral mechanism are responsible for the protective effect. Polyriboinosinic-polyribocytidylic acid did not seem to exert a direct antitumor effect on transplantable polyoma tumors in the rat, indicating that an increase of the immunologic response in the host was responsible for the compound's inhibitory action on polyoma oncogenesis.

- 0686 COMPARATIVE STUDY OF CHROMOSOME ABERRATION IN CELL CULTURES INDUCED BY TUMORIGENIC NON-TUMORIGENIC ADENOVIRUSES. (E.) Zapsepina, (Mechnikov Res. Inst. Virol. Epidem., Odessa, A. G. Stopchanskaya, G. I. Oleinik, N. I. Lys and E. I. Gaidar. *Acta Virol* 14(5):411, 1970.

- 0687 MALARIA AND LYMPHOMA. (E.) Anonymous. *Lancet* 2(7683):1121-1122, 1970.

- 0688 VIRUSES AND BURKITT'S LYMPHOMA. (E.) Anonymous. *Nature* 228(5276):1027-1028, 1970.

- 0689 BURKITT'S LYMPHOMA AND MALARIA. (E.) Wright, D. H. (Med. Sch. Birmingham, England). *Lancet* 2(7678):881-882, 1970.

- 0690 BURKITT'S LYMPHOMA AND MALARIA. (E.) Stewart, A. M. (U. Dept. Social Med., Oxford, England). *Lancet* 2(7681):1031, 1970.

See also:

- * (Rev): 0349, 0350, 0351, 0352, 0353, 0354, 0393
- * (Chem): 0396, 0467
- * (Immun): 0711, 0723, 0730
- * (Epid-Biom): 0757, 0758
- * (Misc): 0792, 0795, 0802, 0811

- 691 ENHANCEMENT OF TUMOR INDUCTION IN MICE BY LONG TERM IMMUNOSUPPRESSION. (E.) Mandel, A. (Case Western Reserve U. Sch. Med., Cleveland, Ohio) and J. J. De Cosse. *Surg Forum* 21:129-131, 1970.

The effect of antithymocyte serum upon the induction of plasmacytomas by Bayol F, a petroleum by-product, was investigated. Young adult mice were given 3 i.p. injections of 0.5 ml of Bayol F at monthly intervals in association with the chronic or acute administration of antithymocyte serum. Mice chronically treated with antithymocyte serum developed plasmacytomas as early as 2 months after Bayol F treatment, and 70% of mice had tumors at 6 months. This effect was not seen in control mice, in mice acutely treated with antithymocyte serum, or in mice immunosuppressed with azathioprine, cyclophosphamide or 250 r of X-ray. Possibly the increased rate of tumorigenesis observed with antithymocyte serum was caused by the alteration of a tumor surveillance mechanism in the host which, in concert with the immunosuppressive effect proper, resulted in an increased rate of oncogenesis.

- 692 DEVELOPMENT OF SEVERE CERVICAL DYSPLASIA UNDER TREATMENT WITH AZATHIOPRINE (IMURAN). (E.) Schramm, G. (Prof. Reis Private Hosp., Munich, Germany). *Acta Cytol* 14(8):507-509, 1970.

The association of the development of severe cervical dysplasia with azathioprine (Imuran) treatment is presented in the case history of a woman who developed dysplasia while under Imuran treatment for autoimmune hepatitis. When the patient (after being on and off Imuran over a 10 month period) underwent a therapeutic abortion at 2 months into pregnancy, only necrotic tissue was found instead of the fetus, and an histological examination 6 months later revealed an advanced borderline lesion or carcinoma *in situ*. A cold knife conization and curettage was performed and the patient recovered without difficulty. Azathioprine treatment was maintained despite the histological findings to prevent progression of the hepatitis, but regular cervical and vaginal smears were scheduled to maintain check for possible recurring cancer.

- 693 CERVICAL DYSPLASIA AND CANCER DEVELOPING IN WOMEN ON IMMUNOSUPPRESSION THERAPY FOR RENAL TRANSPLANTATION. (E.) Kay, S. (Med. Coll. Virginia, Richmond), W. J. Frable and D. M. Hume. *Cancer* 26(5):1048-1052, 1970.

The possibility of an association between cervical dysplastic changes and immunosuppressive therapy for renal transplantation was explored in 28 transplant patients. Patients were aged 11-46 yr, and all had received a minimum of 600 rads to the transplanted kidney, and were maintained on azathioprine and prednisone. Three patients showed cellular abnormalities on Papanicolaou smears. One patient showed mild dysplasia in only 1 smear, but

the other 2 have shown persistent atypia and 1 of the 2 developed *in situ* epithelioma proven by cervical conization. Definite proof that the cervical changes are due to immunosuppressive therapy is lacking; nevertheless, routine screening for cervical dysplasia should be carried out in connection with all transplant operations.

- 0694 LYMPHOSARCOMA IN SIBLINGS, ASSOCIATED WITH CYTOGENIC ABNORMALITIES, IMMUNE DEFICIENCY, AND ABNORMAL ERYTHROPOIESIS. (E.) Freeman, A. I. (Roswell Park Mem. Inst., Buffalo, N. Y.), L. F. Sinks and M. M. Cohen. *J Pediat* 77(6):996-1003, 1970.

A 12-yr-old boy whose sister had died with generalized lymphosarcoma was found to have a lymphosarcoma in the oropharynx. Chromosome studies of a 72-hr peripheral leucocyte microculture showed a group A chromosome which had been replaced by 2 large fragments. Immunological studies showed markedly subnormal circulating levels of IgG, IgA and IgM, and a defect in cellular immunity; hematological findings included ineffective erythropoiesis with low-grade anemia, megaloblastic changes, and multinucleated erythroblasts. The propositus' sister had been similar in physical appearance to the boy, and had had a defect in the thymic-dependent system. Although the symptom constellation exhibited by the propositus and his sister resembles that of Bloom's syndrome, it appears that the reported case represents a new disease entity.

- 0695 SPONTANEOUS DEVELOPMENT OF MAMMARY ADENOCARCINOMA FOLLOWING PROLONGED IMMUNOSUPPRESSION IN THE DOG. (E.) Joseph, W. L. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), F. Melewicz and D. L. Morton. *Cancer Res* 30(10):2606-2608, 1970.

A female mongrel dog being tested for cutaneous hypersensitivity to 2,4-dinitrochlorobenzene underwent immunosuppressive therapy with azathioprine (4 mg/kg/day) for 41 days; the dog developed adenocarcinomas in 2 breasts which were noticed 31 days after initiation of treatment. Simple mastectomy was performed on both breasts and 3½ months later when the dog died, autopsy revealed breast tumors with metastasis to the lung. The case provides further evidence of the association of immunological incompetence and neoplasms.

- 0696 THE EFFECT OF PREDNISOLONE ON RNA- AND DNA-SYNTHESIS IN PHYTOHEMAGGLUTININ-STIMULATED LYMPHOCYTES. (Ger.) Drings, P. (Med. U. Clin. Heidelberg, Germany), E. Fölsch and J. Drews. *Z Ges Exp Med* 153(1):35-50, 1970.

The possibility that prednisolone exercises a preferential inhibitory action upon a ribosomal RNA precursor was investigated. Lymphocyte cultures were taken from healthy patients (without blood dyscrasias) and incubated in a chromosome medium

containing phytohemagglutinin (PHA). Prednisolone hemisuccinate introduced into the culture at a concentration of 30 µg/ml caused a significant inhibition of ³H-thymidine (DNA precursor) incorporation, and the degree of this inhibition was dependent upon the time of introduction of the steroid into the culture medium and the duration of the reaction. Also, directly following PHA stimulation, ³H-uridine incorporation was inhibited. The decrease of RNA synthesis caused by prednisolone was attributed to a decrease in the formation of RNA ribosomal precursor. The fact that the formation of ribosomal RNA in PHA-stimulated lymphocytes was inhibited by prednisolone does not indicate that this mechanism is the only one underlying the catabolic or anabolic effect of prednisolone on lymphocytes.

- 0697 NUCLEAR AND CYTOPLASMIC PROTEIN ACCUMULATION IN PHA-STIMULATED HUMAN LYMPHOCYTES DURING BLASTOGENESIS. (E.) Soren, L. (Karolinska Inst., Stockholm, Sweden). *Exp Cell Res* 59(2):244-248, 1970.

Human lymphocyte cultures were subjected to phytohemagglutinin stimulation, and the increase in nuclear and cytoplasmic mass during blastogenesis was measured by microinterferometry for the purpose of determining nuclear and cytoplasmic protein accumulation in phytohemagglutinin stimulated cells. Both nuclear and cytoplasmic mass increased many-fold during blastogenesis, the increase of cytoplasmic mass being relatively greater than that of nuclear mass; the mean ratio of nuclear mass to cytoplasmic mass for lymphocyte populations before phytohemagglutinin stimulation and 24, 48 and 96 hr after stimulation decreased from 2.9 to 1.7. A considerable part of nuclear mass accumulation occurred before the initiation of DNA synthesis. This is different to nuclear mass increase in tissue cultured cells in logarithmic phase of growth, in which nuclear mass increases parallel to DNA synthesis. However, the mass accumulation after initiation of DNA synthesis is probably related to the increased DNA content of the transformed cell and is similar to accumulation occurring in tissue cultured cells in the logarithmic phase of growth.

- 0698 LYMPHOCYTE TRANSFORMATION IN MEGALOBlastic ANAEMIA: MORPHOLOGY AND DNA SYNTHESIS. (E.) Das, K. C. (Roy. Postgrad Med. Sch., London, England) and A. V. Hoffbrand. *Brit J Haemat* 19(4):459-468, 1970.

The morphology and DNA synthesis of phytohemagglutinin (PHA) transformed lymphocytes from 7 patients with megaloblastic anemia due to deficiency of vitamin B₁₂ or folate were compared to similarly transformed lymphocytes from normal subjects. The mean transformation (78%) was similar for both groups, but the transformed lymphocytes from the patients with megaloblastic anemia were larger with

an increased cytoplasmic-nuclear ratio and a more finely reticulated chromatin pattern. Total DNA content (µg/culture) of the transformed cells was the same in both groups (79.5-84.7), but ³H-thymidine incorporation (cpm/ µg DNA) was significantly higher in the anemic group (5067) than in the controls (2050). In normal transformed lymphocytes deoxyuridine (10⁻¹ µM) reduced ³H-thymidine incorporation to less than 10% of the control value in megaloblastic anemia-transformed lymphocytes; deoxyuridine only reduced incorporation to 65-10% of control values (with 1 culture reduced to 20% of the control). Vitamin B₁₂ (500 ng/culture) partially restored the blocking effect (55-60% inhibition), and folic acid (22 ng/culture) and folic acid (20 ng/culture) completely restored the blocking effect of deoxyuridine (11-19% inhibition).

- 0699 EFFECTS OF ADRIAMYCIN ON HUMAN LYMPHOCYTES STIMULATED WITH PHA *IN VITRO*. (E.)

Massimo, L. (G. Gasslini Dept. Pediat., U. Genoa, Italy), F. Dagna-Bricarelli and A. Fossati-Guglielmoni. *Rev Europ Etud Clin Biol* 15(7):779, 1970.

The effect of adriamycin, an antitumor antibiotic on normal human lymphocytes which were stimulated with phytohemagglutinin *in vitro* was investigated. Lymphocytes from normal donors were cultured with phytohemagglutinin; adriamycin was added in amounts of 0.05-5 µg/ml, and blastogenesis and cytogenetic changes were assayed at different concentrations of adriamycin. Adriamycin inhibited transformation of lymphocytes to blast cells at all concentrations with inhibition approaching 100% as adriamycin concentration approached 3.0 µg/ml. Giant blast cells (50-70µ), basophilic cytoplasm and pyknotic cells began to appear at adriamycin doses of 0.05-0.1 µg/ml. Chromosome aberrations such as breaks, fragments, chromatid exchanges, dicentric rings, aneuploidy and polyploidy were observed even at the lowest concentrations of adriamycin. The mutagenic effect of adriamycin may account for the inhibition of blastogenesis, cellular gigantism and hyperploidy; this effect is the most evident action of the agent on phytohemagglutinin-stimulated lymphocytes.

- 0700 EFFECT OF HAEMATOPOIETIC HUMORAL FACTORS ON PHA-TRANSFORMED LYMPHOCYTES: INHIBITION OF DNA SYNTHESIS IN PHA-STIMULATED LYMPHOCYTE CULTURE AND THE ROLE OF FACTORS CONTROLLING ERYTHROPOIESIS. (E.) Doklen, A. (Frederic Joliot-Curie Natl. Res. Radiobiol. Radiohyg., Budapest, Hungary), V. Varteres and L. Varga. *Haematologia* 4(2):201, 1970.

The effect of hematopoietic humoral factors on lymphocyte cultures stimulated with phytohemagglutinin (PHA) was studied. Lymphocyte cultures were prepared from the blood of normal rabbits and were cultured with PHA for 24-96 hr, and hematopoiesis was assayed by measuring Fe⁵⁹ incorporation by lymphocytes. Cells displaying the morphological characteristics of polychromatic and orthochromatic

ormoblasts were found in the PHA-transformed 72 hr and 96 hr cultures. These cultures also exhibited reticulocytes in different maturation phases. In all PHA-stimulated cultures, heme-synthesis proceeded as measured by Fe^{59} incorporation into hemoglobin, whereas in control cultures, heme-synthesis was not as appreciable. The addition to the cultures of anemic rabbit serum considerably (56-227%) increased Fe^{59} -incorporation into hemoglobin, whereas hypertransfused serum reduced Fe^{59} -incorporation in all cases. Both these humoral factors are known to stimulate or inhibit erythropoiesis, and both had their respective effects when added to cultures 24 hr after the addition of PHA. When added to cultures simultaneously with PHA, however, these humoral factors failed to interfere with heme-synthesis. Peripheral mononuclear cells cultured without PHA apparently did not synthesize heme, and were insensitive to the erythropoietic effect. Mononuclear cells pretreated with PHA, however, began to synthesize heme and became responsive to erythropoietic factors. It was not clear whether all mononuclear cells were responsive in these ways to PHA stimulation.

0701 STUDIES OF FOLATE UPTAKE BY PHYTOHEMAGGLUTININ-STIMULATED LYMPHOCYTES. (E.)
as, K. C. (Roy. Postgrad. Med. Sch., London, England) and A. V. Hoffbrand. *Brit J Haemat* 19(2): 203-221, 1970.

The incorporation of folates by peripheral human blood lymphocytes was studied in cultures stimulated with phytohemagglutinin. The rate of incorporation of tritiated folic acid and of ^{14}C -labeled 5-methyltetrahydrofolic acid by lymphocytes measured in stimulated and unstimulated cultures correlated with rates of DNA and RNA synthesis. In phytohemagglutinin-stimulated cultures, total folate incorporation measured by autoradiography and by liquid scintillation counting was far greater than the incorporation of folates in unstimulated cultures; at 30 hr of incubation, 3×10^6 stimulated lymphocytes incorporated radioactive folates at a rate of 575 cpm, while unstimulated lymphocytes incorporated folates at a rate of 150 cpm at 30 hr. Apparently, growing and dividing cells take up folates more readily than mature non-dividing cells. Temperature affected folate uptake; incorporation at 4°C was 80% less than uptake at 37°C . Folate uptake exhibited saturation kinetics and was inhibited by methotrexate in concentrations higher than 10^{-6}M . Peak rates of folate uptake occurred at 44-48 hr of culture in stimulated cells and preceded peak DNA synthesis by 24 hr, and followed peak RNA synthesis by the same amount of time. However, folate uptake did not appear to be directly related to either RNA or DNA synthesis, for actinomycin D inhibited nucleic acid synthesis without affecting folate uptake. An active transport mechanism may be involved in cellular folate uptake, but the 2 folates tested probably do not share the same uptake pathway, since folic acid did not inhibit the uptake of 5-methyltetrahydrofolic acid by stimulated cells. In addition, the uptake of the

latter compound was significantly impaired in lymphocytes from patients with untreated pernicious anemia, while folic acid uptake in these cells was normal.

0702 THE EFFECT OF CYCLIC AMP AND RELATED COMPOUNDS ON HUMAN LYMPHOCYTE TRANSFORMATION (HLT) STIMULATED BY PHYTOHEMAGGLUTININ (PHA). (E.)
Rigby, P. G. (U. Nebraska Coll. Med., Omaha) and W. L. Ryan. *Rev Europ Etud Clin Biol* 15(7):774-777, 1970.

The effect on human lymphocyte transformation *in vitro* of adenosine-3',5'-monophosphate (cyclic AMP) and related compounds was investigated in lymphocyte cultures stimulated with phytohemagglutinin and in unstimulated cultures. It was found that cyclic AMP and the related compounds 3'-AMP, 2',3'-AMP, 5'-AMP, and 2',3'-guanosine monophosphate and 3',5'-guanosine monophosphate reduced the number of normal lymphocytes in phytohemagglutinin-stimulated tissue culture, the reduction being most evident after 4 days of cultivation. At 3 mg cyclic AMP/ 3 cm^3 of culture, lymphocyte counts were reduced to 49% of control; the same dose of 5'-AMP reduced lymphocyte counts to 36% of normal. Without phytohemagglutinin, treatment with cyclic AMP and related compounds did not markedly reduce the numbers of cells, but the cell counts were invariably reduced in unstimulated cultures. In unstimulated cultures, 3 mg cyclic AMP/ 3 cm^3 of culture reduced lymphocyte counts to only 77% of normal. The role of cyclic AMP and related compounds on lymphocyte proliferation *in vivo* is not clear, although at physiological levels DNA synthesis and mitotic activity are promoted in cultures.

0703 DNA POLYMERASE AND DNA REPLICATION DURING LYMPHOCYTE TRANSFORMATION. (E.) Loeb, L. A. (Inst. Cancer Res., Fox Chase, Philadelphia, Pa.), J. L. Ewald and S. S. Agarwal. *Cancer Res* 30(10): 2514-2520, 1970.

Lymphocytes from the blood of healthy human volunteers were treated with phytohemagglutinin and ^3H -methylthymidine (50 μC), and DNA polymerase and replication activity was observed. An increase of 30- to 150-fold in DNA polymerase activity paralleled in time and magnitude the ability of the cells to synthesize DNA. An increase in DNase activity also paralleled DNA synthesis and the rise in polymerase. The activities of thymidine kinase and thymidine monophosphate kinase multiplied about 2- to 10-fold. In contrast, kinases such as deoxyguanosine monophosphate kinase and guanosine monophosphate kinase, which were present in greater activity, were not increased by phytohemagglutinin. The induction of these enzyme activities by phytohemagglutinin appears to require RNA synthesis. Actinomycin D in concentrations greater than 0.015 $\mu\text{g}/\text{ml}$ abolished the phytohemagglutinin-mediated increases in RNA and DNA synthesis, enzyme activities, and lymphocyte transformation. Smaller amounts of actinomycin (0.005 $\mu\text{g}/\text{ml}$) prevented the induction of DNA

polymerase, thymidine kinase, and thymidine monophosphate kinase, as well as the increase in RNA and DNA synthesis, but did not hinder lymphocyte transformation. Evidently, the stimulation of DNA synthesis depends on the induction of DNA polymerase. In contrast, the morphological changes associated with lymphocyte transformation do not appear to require DNA replication or the increases in enzyme activity associated with this replication.

- 0704 IMMUNOLOGICAL FACTORS IN HUMAN SARCOMAS AND MELANOMAS: A RATIONAL BASIS FOR IMMUNOTHERAPY. (E.) Morton, D. L. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), F. R. Eilber, W. L. Joseph, W. C. Wood, E. Trahan and A. S. Ketcham. *Ann Surg* 172(4):740-749, 1970.

The relationship between the clinical progress of human melanomas and sarcomas and the immune response of the patient to his tumor was investigated. Anti-melanoma antibodies were found in 67% of patients with malignant melanoma, and in 22% of normal subjects. Fewer patients with metastatic melanomas had antibodies (26%) than patients with localized melanoma (89%). All patients undergoing spontaneous regression of melanoma had unusually high anti-melanoma antibody titers. Patients with sarcoma conditions showed similar immune profiles, antibody titers increasing following surgical resection of tumors, and declining in patients with recurrent sarcomas or with pulmonary metastases. In experiments with guinea pigs, the correlation between antibody titers and malignancy was explored further. Living cells from methylcholanthrene-induced liposarcomas were injected into animals which were then immunized with mixtures of BCG and irradiated tumor cells or BCG and living tumor cells. Both treatments significantly inhibited growth of the i.m. injected liposarcoma, but the living cells were more effective inhibitors than irradiated cells. Thirty days after liposarcoma injection, 27 of 28 control guinea pigs bore tumors, while 12 of 20 animals treated with irradiated cells and BCG, and none of 20 treated with living tumor cells and BCG, bore tumors. In studies with human patients, 12 patients with malignant melanoma, skeletal and soft tissue sarcoma were given immunotherapy. All patients treated with tumor cells and BCG exhibited rising titers of anti-sarcoma antibodies, and a temporary decrease in the growth rate of pulmonary metastases was observed in 2 patients following immunotherapy. Immunotherapy using BCG and tumor cells apparently may be indicated as an adjunct treatment with surgery for melanoma and sarcoma conditions.

- 0705 *SACCHAROMYCES CEREVISIAE*, AN IMMUNOLOGICAL FACTOR IN THE INHIBITION OF SARTORELLI'S TG 180 ASCITES SARCOMA TRANSPLANTATION IN MICE. (Fr.) Vermeil, C. (Fac. Med. Nantes, France) and O. Morin. *C R Acad Sci* 271(3):378-380, 1970.

Complete protection against the peritoneal graft a TG-180 ascitic sarcoma in mice was obtained by inoculation of cycloheximide-modified *Saccharomyces cerevisiae* (Charron's strain). The yeast (200 mg) were first treated with cycloheximide (0.01% physiological solution with 2% glucose) for 1 hr at 25°C and then inoculated into a sarcoma-bearing mouse, i.p. The animal was sacrificed 1 hr later and the ascites, containing sarcoma and yeast cells, was recovered, twice frozen and thawed, and then centrifuged to partially separate yeast from the tumor cells. These yeast cells were then inoculated into 3 mice i.p. for 4 times at weekly intervals, and the treated mice along with controls were inoculated with 1000-2000 sarcoma cells each, i.p., 1 wk following the last yeast cell treatment. No tumors developed in the pretreated mice while usual sarcomatous evolution occurred in the control animals.

- 0706 PROPERTIES OF SARCOMAS INDUCED BY FERRIDEXTRAN SPOFA IN THE INBRED RAT STRAIN AVN: I. TRANSPLANTABILITY OF FEDEX-AVN TUMOURS *VIVO* AND KARYOLOGICAL AND MORPHOLOGICAL PROPERTIES OF THE CELL LINE AFTER EXPLANTATION *IN VITRO*. (E) Kren, V. (Fac. Gen. Med. Charles U., Prague, Czechoslovakia), D. Krenova and O. Stark. *Neoplasia* 17(4):329-337, 1970.

The morphology, karyotype, and transplantability of sarcomas induced in strain AVN rats by i.m. administration of Ferridextran Spofa were investigated. The tumors were spinocellular sarcomas with some expression of fibroid production; after 7 months *vivo* passaging, the tumor presented the appearance of a pleomorphic malignant mesenchymal neoplasm. Tumors were transplantable in the original rat strain, and the rate of implanted tumor growth was related to the elapsed time from induction of transplanted tumors. Tumors transplanted earliest after induction grew most slowly. Rats of the allogeneic strains BP, LEW, and WP rejected tumor transplants and produced anti-tumor hemagglutinins. Rat strains having the H-1^a positive allele sustained tumor transplants in only negligible numbers (4 of 14 H-1^a positive rats). When doses of 5×10^5 or 1×10^5 tumor cells were administered to semi-syngeneic hybrid rats the time of survival of the rats was longer than the time of survival of syngeneic rats. Karyotypically, the tumor was high polyploid with most mitoses having chromosome complements of 55-75 chromosomes. The low growth ability of the tumor on H-1^a positive and semi-syngeneic rats may be accounted for by allogeneic inhibition.

- 0707 ANTIGENIC CHANGES IN GASTRIC CANCER. Ortiz De Landazuri, M. (Fac. Med. U. Navarra, Spain) and A. Chordi. *Rev Clin Espagn* 118(5):441-446, 1970.

Immunoelectrophoretic data on gastric cancer antigens were compared to those obtained with normal gastric tissues (duodenal ulcer patients) and with antigens from embryonic tissues (less than 5 months).

of gestation). Normal gastric tissue extracts had 20 immunologically different antigens of which 7 were in common with serum, 2 were in common with other organs (thyroid) and 11 were organ-specific. The gastric cancer tissue extracts had 20 antigens of which 10 were in common with serum, 2 were in common with other organs (thyroid) and 8 were gastric cancer-specific. Complete disappearance of normal organ-specific G133, G113 and G90 antigens and considerable decrease of organ-specific G53, G46a, G46b and G46c occurred in the cancer tissue, while the number of serum antigens was increased (from 7 to 10). Common for both normal and cancer tissues were G12, G28, G85 and G100 antigens. The presence of 4 antigens, specific for cancer tissue, was ascertained in the total cancer tissue homogenate and their distribution in subcellular fractions was determined. These were designated as N46a, N46b (predominant in the soluble cytoplasmic, mitochondrial and microsomal fractions) and N28 and N80 (predominant in the total cancer tissue homogenate). A distinct precipitation band (electrophoretic mobility=46) was noticed in the total fetal tissue homogenate, which was in common with the 46b cancer tissue antigen and was designated as the carcinoembryonic 46b antigen.

0708 DIFFERENT LOCATIONS OF CARBOHYDRATE-CONTAINING SITES IN THE SURFACE MEMBRANE OF NORMAL AND TRANSFORMED MAMMALIAN CELLS. (E.) Sela, B. A. (Weizmann Inst. Sci., Rehovoth, Israel), H. Lis, N. Sharon and L. Sachs. *J Membrane Biol* 3(3): 267-279, 1970.

The action of soybean agglutinin (SBA) and its receptor site on the surface membrane were studied in normal and transformed (by polyoma virus, SV40, or adenovirus) human mouse, rat, and hamster cell lines. The transformed human, mouse, and rat cells were agglutinated by SBA (50-100 µg/ml), but the transformed hamster cells and all of the normal cell lines were not agglutinated. Normal cells became agglutinated by SBA after trypsin or pronase treatment (10 µg/ml for 5 min), but transformed hamster cells could be agglutinated only after prolonged pronase treatment (30-90 min). N-Acetyl-D-galactosamine (0.15 µmoles/ml) inhibited the agglutination by 50%, indicating that N-acetyl-D-galactosamine-like saccharides are part of the receptor sites for SBA on the surface membrane and exist in a cryptic form in normal human, mouse, and rat cells and become exposed in transformed cells (although they become less accessible in transformed hamster cells). Wheat germ agglutinin and Concanavalin A agglutinin interacted with different receptor sites (N-acetyl-D-glucosamine-like and α-D-glucopyranoside-like sites, resp.), and the sites for the different agglutinins became exposed in normal hamster cells after trypsin (1 µg/ml) treatment for 1, 3 and 5 min for wheat germ, Concanavalin A and SBA, resp.

0709 IMMUNOLOGICAL STUDIES ON YOSHIDA SARCOMA CELLS: II. CELLULAR LOCALIZATION OF HETEROLOGOUS ANTI-YOSHIDA SARCOMA CELL ANTIBODIES AND IMMUNOHEMOLYTIC ANEMIA INDUCED BY THEIR INJECTIONS

IN THE RAT. (E.) Sugiyama, H. (Fac. Med. U. Tokyo, Japan) and T. Kuroyanagi. *Japan J Exp Med* 40(3): 191-199, 1970.

The effect of absorption of heterologous anti-Yoshida sarcoma (YS) serum with YS antigens on the penetration of anti-YS cell serum into viable YS cells was investigated in immunofluorescence tests. Anti-YS serum was prepared in rabbits; the YS cell antigens fractionated for study were the nuclear fraction and the insoluble sediments of supernatants derived from centrifugation of YS cell homogenates. When viable YS cells were incubated with heterologous anti-YS serum without complement, anti-YS serum did not penetrate the viable cells, while penetration did occur in the presence of complement. The absorption of serum with supernatants of YS cells had no effect on its penetration into YS cells in the presence of complement. However, when anti-YS serum was absorbed with the insoluble sediment of YS cells or normal rat red cell membranes, penetration of serum into YS cells did not take place. These results were thought to indicate that antigens responsible for the antibody which plays the major role in anti-YS serum penetration were present in the insoluble sediment of YS cells, and that these antigens had common antigenicity with normal rat red cell membranes. The hypothesis was tested by injecting Donryu rats with 0.5 ml of anti-YS cell serum or with 0.5 ml of serum which had been absorbed with the insoluble sediment of YS cell homogenates. The former treatment, but not the latter, induced immunohemolytic anemia in the rats. Ferrokinetic studies using ⁵⁹Fe showed a prolongation of the generation cycle of nucleated erythroid cells in rats injected with anti-YS cell serum. The anemia and the prolongation of the generation cycle may have been due to incomplete antibodies present in the anti-YS cell serum.

0710 IMMUNOLOGIC AND IMMUNOTHERAPEUTIC STUDIES WITH HUMAN SARCOMAS. (E.) Eilber, F. R. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and D. L. Morton. *Surg Forum* 21:127-129, 1970.

Antisarcoma antibody titers were assayed in 35 patients with skeletal and soft tissue sarcomas to determine whether there was a correlation between antisarcoma antibody titer, delayed cutaneous hypersensitivity to the sarcoma antigens, and the clinical course of the malignant disease. A good correlation was found between antisarcoma antibody titer and the clinical course. High antibody titers (1/32 or greater) were found in patients surviving longer than 3 yr following primary treatment for sarcoma. Elevated titers were found in patients remaining tumor-free following surgery, while patients developing recurrence of tumors exhibited declining antibody titers. Immunization with 75 x 10⁶ irradiated (15,000 r) autologous tumor cells reversed the decline of circulating antibodies. Antibody activity was found to be associated with immunoglobulins of types IgG and IgM. In 7 patients having elevated antibody titers following immunization delayed cutaneous hypersensitivity to 1 x 10⁶ autologous irradiated tumor cells and ether soluble sarcoma antigen was noted.

- 0711 A COMPLEMENT BINDING REACTION TO DEMONSTRATE COMMON ANTIGEN COMPONENTS IN THE LEUKEMIA VIRUS OF VARIOUS MAMMALS. (Ger.) Schäfer, W. (Max Planck Inst. Virus Res., Tübingen, Germany), J. Lange, L. Pister, E. Seifert, F. De Noronha and F. W. Schmidt. *Z Naturforsch* 256(9):1029-1036, 1970.

The prevalence of leukemia viruses in various animal species suggests that malignancy in man could also be attributed to this virus. The antigen formation of this RNA containing complex virus is reminiscent of the influenza viruses. Serological comparison of avian leukemia virus (ALV), murine leukemia virus (MLV), feline leukemia virus (FLV) and hamster leukemia virus revealed the presence of an interspecies specific (gs-interspecies) antigen except in case of ALV. Rabbit immunization with purified MLV-gs-antigen allowed isolation of an antiserum (R-gs-serum) which precipitated specifically the MLV and FLV gs-antigens. The complement binding tests with R-gs-rabbit serum proved to be 5 times more sensitive against FLV; preliminary investigations with cattle and human material using this serum gave results which seemed to be positive.

- 0712 PRELIMINARY COMMUNICATION ON THE EVIDENCE OF ANTIBODIES AGAINST VARIOUS BLAST TYPES IN PERSONS EXPOSED TO ACUTE PEDIATRIC LEUKEMIAS. (Ger.) Ziantl, F. (U. Child. Clin., Jussuf Ibrahim, Jena, Germany), G. Aurich and W. Plenert. *Folia Haemat* 94(1):31-40, 1970.

The sera of 39 contact persons, consisting of physicians and other staff personnel who had been in contact with leukemic children, as well as the sera of the children's parents, were tested for antibodies against acute infant leukemia by immunofluorescent techniques. The target cells were taken from 3 different children with: monocytoid blasts, "paramyelo blasts", and "parablasts", resp. A positive membrane fluorescence with the 3 cell types was found among the tested contacts in varying amounts. The most frequent positive reactions were in response to the application of "parablasts". The control tests performed in subjects who had never been exposed to leukemia patients were all negative.

- 0713 BLAST CELL LEUKAEMIA ASSOCIATED WITH IgA PARAPROTEINAEMIA AND BENCE JONES PROTEIN. (E.) Thijs, L. G. (Dept. Intern. Med., Free U., Amsterdam, Netherlands), W. Hijmans, W. Leene, O. G. Muntinghe, R. N. I. Pietersz and J. E. Ploem. *Brit J Haemat* 19(4):485-492, 1970.

Blast cell leukemia associated with IgA paraproteinemia and Bence Jones protein was illustrated in the case of a 47 yr-old female patient. The patient was diagnosed as having myeloblastic leukemia, with IgA kappa paraproteinemia and with Bence Jones kappa proteins in her serum and urine. Although it appeared that two neoplastic conditions involving both the myelocytic and the plasma cellular series were in effect, electron microscopy and immunofluorescence tests revealed that the blast cells belonged to the plasma cell series. Accordingly,

the diagnosis was changed to myeloma with leukemia and this diagnosis was borne out at autopsy which revealed a typical "myeloma kidney" condition. cases of blast cell leukemia care should be taken to search for paraproteins.

- 0714 HL-A ANTIGENS ON LEUKAEMIC CELLS. (E.) Pegrum, G. D. (Charing Cross Hosp. Med. Sch., London, England), I. C. Balfour, C. A. and V. L. Middleton. *Brit J Haemat* 19(4):493-498, 1970.

The frequencies of HL-A antigens in leukemic cell lines was investigated. Antigen assays were carried out in blood from 26 patients with leukemic conditions with alloantisera which recognized 13 HL-A antigen specificities. Increased incidences of HL-A 1, HL-A 3, HL-A 7, HL-A 8 and Lc19 antigens were found, the most notable being the increase in HL-A 3 antigen frequency from 25% in normal subjects to 57% in the leukemia patients. A slight decrease in the frequency of HL-A 2 antigen was found, the frequency in normal controls being 49% and the frequency in leukemic patients being 34.5%. These findings suggest that leukemic cells either react differently to the alloantisera or that additional tumor-specific antigens are present on the cells. It is also possible that a genetic predisposition to develop leukemia characterizes people with the antigenic configurations.

- 0715 SPECIFICITIES OF γ A-MYELOMA PROTEINS. Tominaga, K. (Fac. Med. Kyushu U., Fukuoka, Japan). *Acta Haemat Jap* 33(1):85-86, 1970.

The relationship between the subclass and polypeptide chain structure was examined in 5 purified myeloma proteins with identified subclasses. The lowest protein concentrations (mg/ml) for positive reaction against γ A1- and γ A2-specific antisera were 0.23 and 15 for Gb, 0.16 and 2.5 for Hr, 0.16 for Kt, 0.23 and 1.9 for Fr, and 0.15 and 0.15 for Kw subclasses. L chain dimer dissociation was observed in Hr. Reduced γ A-myeloma protein Hr transformed more slowly than its oxidized counterpart indicating a difference from others in the polypeptide chain structure. Kw showed a slight tendency toward chain dissociation in disc electrophoresis, while L chain dissociation was seen in Fr, although the protein reacted against anti- γ A2 antiserum in relatively low concentration.

- 0716 THE MECHANISM AND SIGNIFICANCE OF PERIODIC PLOIDY-ALTERATIONS IN THE MOUSE MYELOMA MSPC-1. (E.) Moriwaki, K. (Natl. Inst. Genet., Misima, Japan) and H. T. Imai. *Acta Haemat Jap* 33(1):67-78, 1970.

The cytological mechanisms and immunological significance of the periodic ploidy changes from diploid to tetraploid in several transplantable myelomas of the mouse myeloma, MSPC-1, over a 100 day period were studied with marker chromosomes and autoradiography in BALB/c mice. Pretreatment of the cells with γ -irradiation (200 r) decreased the tumor

duction period by 2 days but did not create any significant differences in the ploidy changes. Tetraploid cells were formed from diploids through the failure of cytokinesis and the fusion of binuclei in the binucleate-cell stage, while diploidization occurred through a degeneration of the tetraploid cells (with an unexplained cytological mechanism) and a minor fraction of existing diploid cells resumed active proliferation. The growth pattern in the MSPC-1 myeloma (where the active diploid population maintained a few repressed diploids) was similar to the pattern of active plasma cells capable of producing antibody and memory cells and suggests that the mechanism of antibody formation may be approached through the cytogenetics of the maturing antibody forming cells.

- 0717 LEUCOCYTE PHENOTYPES IN HODGKIN'S DISEASE. (E.) Zervas, J. D. (Roy. Natl. Orthop. Hosp., Brockley Hill, Stanmore, Middlesex, England), I. W. Delamore and M. C. G. Israels. *Lancet* 2(7674):634-635, 1970.

Hodgkin's disease patients (27) and normal controls were typed for 8 HL-A antigens (HL-A1, HL-A2, HL-A3, HL-A5, HL-A8, LA-4, LC-17, and LC-20) and their leukocyte phenotypes were determined to investigate the occurrence of HL-A specificity associated with this disease. Hodgkin's disease patients exhibited a greater frequency of HL-A5 antigen specificity with antiserum D-66-6222VI (63%) than the controls (20%). Antiserum Kieffer, which is supposed to have HL-A5 specificity, gave 86% positive reactions with leukocytes from Hodgkin's disease patients and 90% positive tests with leukocytes of healthy patients, indicating that this antiserum is not monospecific. Antisera HL-A8 and LC-17 also showed higher positive reactions with leukocytes of Hodgkin's disease patients (37% and 33%, resp.) compared to healthy patients (25% and 16%, resp.). A correlation appears to exist between Hodgkin's disease and HL-A phenotype.

- 0718 LEUCOCYTE ANTIGENS IN HODGKIN'S DISEASE. (E.) Forbes, J. F. (Dept. Surg., U. Melbourne, Australia) and P. J. Morris. *Lancet* 2(7678):849-851, 1970.

Microlymphocytotoxic techniques using between 60-120 cytotoxic antisera were employed in testing the blood of 110 patients (in groups of 35 and 75) for the frequency of an antigen designated 4c by Amiel. An antigen previously known as 4c was found in 56% and 45%, resp., of the patients in the 2 series, compared with 25% in the normal Australian population. This difference appears to be due to an increased frequency of an included antigen, W5. Family studies have shown a normal segregation of antigen W5, but have not as yet revealed any abnormal frequency of haplotypes. The association between Hodgkin's disease and the 4c antigen may indicate that the pathogenesis of Hodgkin's disease is connected with genetic or viral factors.

- 0719 CLONAL EVOLUTION IN TWO PATIENTS WITH AUTOIMMUNE DISEASE AND LYMPHORETICULAR NEOPLASIA. (E.) Adam, M. (U. West Indies, Jamaica), M. J. Thorburn, W. N. Gibbs, S. E. H. Brooks and B. Hanchard. *Brit J Cancer* 24(2):266-276, 1970.

A 36-yr-old man and a 48-yr-old woman diagnosed as having lymphosarcoma with possible autoimmune disease and autoimmune disease with possible lymphosarcoma, resp., are described. In both cases, circulating mononuclear cells showed phytohemagglutinin responsiveness (mitotic rate of 25%). Cytogenetic studies on peripheral blood cultures from the male patient showed most of the cells had hyperdiploid complements with a modal number of 48 in 50% of the cells; with bone marrow 12% of the cells had 47-50 chromosomes. Peripheral blood cultures from the woman patient had cells of two types, a normal female diploid line (40%) and a tetraploid line (60%). Large numbers of chromosome (over 90) were observed in the latter cells. The findings appear to support the hypothesis that an abnormal clone of immunocytes may be implicated in both autoimmune disease and leukemia.

- 0720 BIOSYNTHESIS OF THE CARBOHYDRATE PORTION OF IMMUNOGLOBULINS: KINETICS OF SYNTHESIS AND SECRETION OF ^3H -LEUCINE-, ^3H -GALACTOSE- AND ^3H -MANNOSE-LABELED MYELOMA PROTEIN BY TWO PLASMA-CELL TUMORS. (E.) Melchers, F. (Max Planck Inst. Molec. Genet., Berlin, Germany). *Biochem J* 119(4):765-772, 1970.

The kinetics of incorporation of ^3H -leucine, ^3H -mannose, and ^3H -galactose into the carbohydrate portion of immunoglobulins were studied in cell suspensions of 2 myeloma plasma-cell tumors, MOPC 21 which produces and secretes IgG myeloma protein and MOPC 46 which produces and secretes a κ -type light chain with attached carbohydrate. In the first 3 hr of ^3H -leucine incorporation, approximately 23% of the total acid-precipitable radioactivity was myeloma protein, and 90% of this labeled protein synthesized within the plasma cell was secreted. More than 90% of the ^3H -galactose was incorporated into galactose residues of both intracellular and secreted protein, while ^3H -mannose was incorporated significantly (90%) into glucosamine and mannose residues of intracellular protein and into glucosamine, mannose, and fucose residues of secreted protein. Addition of some of the carbohydrate residues appears to be a stepwise process with mannose and glucosamine residues added early and fucose residues added near the final stages of secretion from the plasma cell.

- 0721 RETROGENETIC EXPRESSION: THE REAPPEARANCE OF EMBRYONAL ANTIGENS IN CANCER CELLS. (E.) Stonehill, E. H. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.) and A. Bendich. *Nature* 228(5269):370-372, 1970.

The possible universal appearance of embryonic antigens in cancer tissues was investigated. Whole

mouse (Swiss) embryo extracts were used as the immunizing antigen to prepare antisera in the rabbit, and sera were screened (agar diffusion and immunoelectrophoresis) against prepared extracts of normal embryonic, neonatal, and adult antigens and against extracts of malignant cells of 72 tumors from mice of 18 different inbred strains (viral or chemical induction, irradiation, or spontaneous malignancies). Serum against 9 day mouse embryo, after absorption with normal adult organs, reacted with extracts of all 72 tumors, and with extracts of normal embryo or normal adult skin, but not with other normal adult tissues. In the mouse, such reappearance and persistence of embryonal antigens (retrogenetic expression) in malignant cells appear to be universal phenomena. It could not be determined whether retrogenetic expression is a cause or an effect of cancerigenesis.

- 0722 LYMPHOCYTIC REACTION AROUND PRIMARY AND METASTATIC MELANOMAS. (E.) Payan, H. M. (Clarksburg VA Hosp., West Virginia U., Morgantown), E. F. Gilbert and W. H. Jacobs. *Southern Med J* 63(11):1350-1352, 1970.

Lymphocytic reactions occurring in the vicinity of primary and metastatic melanomas were investigated in 15 primary tumors and in 25 metastases. Metastatic melanomas studied involved the breast, head and neck, and upper and lower extremities. Pigmentation was present in 93% of primary tumors and in 56% of metastases, while necrosis was minimal in both primary and metastatic lesions. A definite lymphocytic infiltrate was found in and around 67% of the primary tumors, and in none of the metastases. Lymphocytic reactions in primary tumors were classified as "moderate". Eighty percent of metastases were to the lungs and lymph nodes, while 60% affected the liver, central nervous system and kidneys. The presence of a lymphoid reaction in and around primary melanomas may be an indication that an immunologic response or defense mechanism exists in the tumor-body interaction.

- 0723 HEPATITIS-ASSOCIATED ANTIGEN IN UGANDAN PATIENTS WITH HEPATOCELLULAR CARCINOMA. (E.) Vogel, C. L. (Uganda Cancer Inst., Kampala), P. P. Anthony, N. Mody and L. F. Barker. *Lancet* 2(7674):621-624, 1970.

Serum was collected from 45 Ugandan patients with hepatocellular carcinoma and 122 controls in an effort to detect the presence of hepatitis-associated antigen. Eighteen of 45 (40%) patients and 4 of 122 (3%) control patients had positive complement-fixation tests for hepatitis-associated antigen. There was a tendency for hepatitis-associated antigen-positive individuals with hepatocellular carcinoma to be α -fetoprotein positive and to have underlying cirrhosis of the "posthepatic" type. Young patients tended to be hepatitis-associated antigen-positive more frequently than old patients. The presence of the hepatitis-associated antigen in liver cancer patients suggests that the etiology and pathogenesis of hepatocellular

carcinoma in Uganda may be associated with an antecedent viral-hepatitis infection, or that hepatocarcinoma patients are more susceptible to hepatitis or to persistence of the antigen in their blood.

- 0724 AUSTRALIA ANTIGEN AND PRIMARY LIVER CANCER. (E.) Moertel, C. G. (Mayo Clin., Rochester, Minn.), G. J. Gleich and E. W. Hull. *Amer J Dig Dis* 15(11):983-985, 1970.

A study designed to determine the frequency of Australia antigen in American patients with primary liver cancer is described. Of 35 patients with liver cancer, none had detectable Australia antigen. Hepatic neoplasms included in the patient series were hepatoma, mixed hepatic carcinoma, primary hepatic hemangioendothelioma, and cholangiocellular carcinoma. Of 31 control patients with nonmalignant liver conditions 3 exhibited Australia antigen (acute hepatitis, chronic active liver disease and Laennec's cirrhosis with primary carcinoma of the bile duct). Although the population studied was without Australia antigen, the possibility of an etiologic viral factor in liver carcinoma cannot be ruled out.

- 0725 COOPERATION OF IMMUNE LYMPHOID CELLS AND MACROPHAGES IN TUMOUR IMMUNITY. (E.) Evans, R. (Chester Beatty Res. Inst., Belmont, Sutton, Surrey, England) and P. Alexander. *Nature* 228(5272):620-622, 1970.

Cells of a murine lymphoma tumor were introduced into cultures of peritoneal exudate cells and macrophages prepared from mice resistant and sensitive to the murine lymphoma. Although macrophages from non-immune mice had no effect on the growth of tumor cells, growth was completely inhibited by immune-mouse macrophages. The ratio of macrophages to tumor cells was 40:1; however, cytotoxic effects were observed with macrophage-tumor cell ratios as low as 10:1. It was also found that normal macrophages, previously non-cytotoxic, become cytotoxic towards lymphoma cells following incubation with spleen cells from immune mice. The findings suggest that the success of a host in containing a tumor depends on the co-presence of immune lymphocytes and macrophages.

- 0726 UREA-EXTRACTABLE ANTIGENS IN NORMAL EPIDERMIS AND NEOPLASTIC MOUSE EPIDERMIS. Carruthers, C. (Roswell Park Mem. Inst., Buffalo, N. Y.). *Oncology* 24(5):321-334, 1970.

The antigenic relationships between the urea-extractable proteins of mouse epidermis, papillomas and squamous-cell carcinomas (induced by 0.3% methylnitrosourea) were investigated. Antisera against normal mouse epidermis, papillomas and carcinomas were prepared in rabbits, and the relationship between these antisera and the antigens of the 3 tissues were studied by immunodiffusion in agar. Normal mouse epidermis had urea-extractable antigen (UEA) in much larger amounts than did urea extracts of papillomas and squamous-cell carcinoma. Papillomas and carcinomas have several UEA in common; papilloma and

cinoma antigens were present in normal epidermis, but in small amounts. In the immunodiffusion tests, the amount of papilloma and carcinoma UEA required in order to inhibit precipitin band formation between normal skin UEA and the normal skin antigens was, resp., 16 and 14 times as great as that of the normal skin UEA, a finding which appears to suggest that there is a change in the antigenic determinants in the UEA of benign or malignant growth, or that these tissues are deficient in epidermal UEA.

0727 TUMOR IMMUNITY PRODUCED BY THE INTRADERMAL INOCULATION OF LIVING TUMOR CELLS AND LIVING *MYCOBACTERIUM BOVIS* (STRAIN BCG). (E.) Zbar, B. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), I. Bernstein, T. Tanaka and H. J. Rapp. *Science* 170(3963):1217-1218, 1970.

The specific tumor immunity produced by inoculation of guinea pigs with living tumor cells and living *Mycobacterium bovis* (strain BCG) was observed. Guinea pigs received 1.5×10^6 cells of ascites tumor line number 10 (lethal dose of 10^5 cells) and 6×10^6 bacteria cells (which produced an initial inflammatory reaction). Immunity was tested by a subsequent (31-35 days later) injection of 10^6 tumor cells. Animals immunized in this way were capable of suppressing the intradermal growth of tumor cells in a challenge inoculation ten times greater than the lethal dose. Tumor nodule size at 8 days following challenge in immunized animals was 0 and 23 mm² in control animals. Protected animals remained tumor free for 3 months after the initiation of the experiment. Immunization with BCG alone did not impair the growth of line 10 tumor cells. Animals immunized with ascites tumor line 1 did not suppress the growth of line 10 tumor cells.

0728 TRANSFER OF TUMOR IMMUNITY WITH RIBONUCLEIC ACID. (E.) Deckers, P. J. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and Y. H. Pilch. *Surg Forum* 21:124-126, 1970.

The transfer of tumor-specific immunity by isologous immune RNA within a syngeneic system and the efficacy of systemic administration of immune RNA without cells in transfer of immunity was investigated. RNA was extracted from the spleens of rats which had been immunized by growth and amputation of a syngeneic benzpyrene-induced fibrosarcoma; the RNA was incubated with normal spleen cells. Untreated rats were injected i.v. with 5×10^7 to 5×10^8 RNA-incubated spleen cells for 3 days; 24 hr following the last RNA-spleen cell injection, all animals received 10^5 tumor cells. Control rats were given tumor cells alone or tumor and spleen cells preincubated with RNA from spleens of untreated rats. In the rats receiving syngeneic spleen cells incubated with immune RNA, tumors measured about 4.8 cm³, while rats receiving tumor cells and spleen cells preincubated with RNA from spleens of untreated rats developed tumors measuring 23.8 and 13.9 cm³, resp. In another experiment, rats received 10^4 tumor cells and on the same day and on alternate days for 10 days were injected with a mix-

ture of dextran sulfate and RNA prepared from lymph nodes and spleens of immunized guinea pigs. Control groups received tumor cells alone, tumor cells with dextran sulfate and RNA extracted from lymph nodes and spleens of unimmunized guinea pigs, or tumor cells and dextran sulfate. Rats receiving immune RNA from guinea pig mixed with dextran sulfate showed inhibition of tumor development (5/20 rats developed tumors) compared with rats receiving tumor cells alone (19/21 rats developed tumors), rats receiving RNA from spleens of unimmunized guinea pigs (15/21 rats developed tumors) and rats receiving tumor cells and dextran sulfate (11/11 rats developed tumors).

0729 THE SERUM PARAPROTEIN LEVEL RELATED TO THE NUMBER OF PLASMACYTOMA-5563 CELLS IN C3H MICE. (E.) Fakhri, O. (Roy. Postgrad. Med. Sch., London, England) and J. R. Hobbs. *Brit J Cancer* 24(2):395-397, 1970.

0730 THE EFFECT OF PHYTOHEMAGGLUTININ ON BURKITT'S LYMPHOMA CELL CULTURES. (Sp.) Sanchis-Bayarri Lahoz, V. (Valencia, Spain) and V. Sanchis-Bayarri Vaillant. *Medicamenta* 54(478):87-91, 1970.

0731 AN ANTIGEN IN THE URINE OF CANCER PATIENTS: DETECTION BY IMMUNO-ELECTROPHORESIS. (Fr.) Aron, M. (Fac. Med. Strasbourg, France). *C R Acad Sci* 271(5):559-562, 1970.

0732 THE ENHANCEMENT OF ANTITUMOR IMMUNITY BY ARTIFICIAL HAPTENE-CONJUGATED ANTIGENS. (Rus.) Korosteleva, T. A. (USSR Min. Publ. Hlth., Leningrad), A. T. Zasyepka and A. B. Orlov. *Vop Onkol* 16(7):62-67, 1970.

0733 LYMPHOCYTE CULTURES FROM NORMAL AND LYMPHOPROLIFERATIVE DISEASE PATIENTS: PHYTOHEMAGGLUTININ CONSUMPTION. (It.) Tognella, S. (Inst. Path. Spec. Med., U. Cagliari, Italy), G. S. Del Giacco, G. Mantovani, P. E. Manconi and V. Grifoni. *Boll Soc Ital Biol Sper* 46(6):311-315, 1970.

0734 STUDY OF IMMUNOGLOBULINS IN MALIGNANT IMMUNOPROLIFERATIVE DISEASES. (Sp.) Ferragut, A. (Hosp. Santa Cruz y San Pablo, Barcelona, Spain), J. De Balanzo. *Rev Clin Espagn* 117(4):343-348, 1970.

See also:

- * (Rev): 0354, 0355, 0356, 0357, 0358, 0360, 0361, 0362, 0391, 0393
- * (Chem): 0394, 0409, 0434, 0454, 0455, 0456, 0468, 0471
- * (Viral): 0551, 0552, 0559, 0573, 0577, 0578, 0579, 0582, 0595, 0596, 0598, 0599, 0616, 0617, 0618, 0623, 0624, 0635, 0652, 0653, 0655, 0656, 0657, 0669, 0670, 0671, 0676, 0679, 0682

- 0735 CONTRIBUTIONS TO THE HISTOGENESIS OF BASAL CELL CARCINOMA. (E.) Brody, I. (Karolinska Hosp., Stockholm, Sweden). *J Ultrastruct Res* 33(1-2):60-79, 1970.

The morphology of tumor cells from superficial basal cell carcinoma in 17 patients bearing lesions on the trunk was studied under the electron microscope. In the tumor buds of superficial basal cell carcinoma, 2 basic cell types were found: cells in which the cytoplasm forms only a small zone around the nucleus (type I), and cells in which the cytoplasm constitutes a larger proportion of the cell material (type II). The major portion of tumor bud cells was composed of cells of type I. Due to differences in nuclear and cytoplasmic opacity and density 3 subtypes of cells, termed dark, intermediate and light, were seen in both types. The nuclei differed with respect to opacity and density of the nuclear matrix. The differences in opacity and density of the cytoplasm were due to differences in the number and density of the ribosomes and in the occurrence of a fairly opaque substance between the ribosomes. The mitochondria were on the whole less numerous than in normal adult epidermis, whereas the α -cytomembranes were quite numerous and the Golgi apparatus was rather well developed. The fibrils were very few compared with those in the normal adult human epidermis. The desmosomes were considerably reduced in number, whereas the nexuses were numerous and usually of some length. Along large stretches the cells lay close together. Squamous cell foci were observed in repeated studies, and they appeared to correspond to the light cells of type II. The presence of 2 main types of cells in superficial basal cell carcinoma supports the theory of Pinkus that basal cell carcinoma originates from adult but pluripotent cells.

- 0736 THE DNA CONTENT OF ALVEOLAR MACROPHAGES AND A SO-CALLED ALVEOLAR CELL CARCINOMA. (E.) Pfitzer, P. (Inst. Path., U. Dusseldorf, Germany). *Acta Cytol* 14(8):479-485, 1970.

Sputum smears from healthy patients and from a patient with large cell carcinoma of the giant cell type affecting the lung were examined microscopically to investigate the DNA content of alveolar macrophages in the sputum. Dumbbell-shaped nuclei were frequently seen but only a few of them divided amitotically into small twin nuclei of more or less unequal size with corresponding pseudo-haploid DNA values. Tumor cells in the lung cancer patient imitated atypical alveolar macrophages with phagocytosis and vacuolated cytoplasm. The DNA content of the nuclei corresponded to 2, 3-4, 6-8, 12, 14, 20 and 22 C. In many cells identical nuclei were lying very close together, probably as a consequence of short mitotic spindles. The fusion of a varying number of such nuclei may explain DNA values such as 3, 14, 20 and 22 C. The DNA variability did not appear to be due to alterations in synthesis or necrosis.

- 0737 INFLAMMATORY PAPILLARY HYPERPLASIA OF ORAL MUCOSA: REPORT OF 341 CASES. (E.) Bhaskar, S. N. (Walter Reed Army Med. Ctr., Washington, D.C.), J. D. Beasley, III and D. E. Cutright. *J Amer Dent Ass* 81(4):949-952, 1970.

A survey of 341 cases of inflammatory papillary hyperplasia was conducted to describe the natural history of the lesion which affects the oral mucosa and occurs most often in the maxilla. The majority of cases are associated with dentures; and the average age of patients suffering from inflammatory papillary hyperplasia is 40.2 years. The lesion shows pseudoepitheliomatous hyperplasia, keratin cysts, and keratin pearls; however dyskeratosis is not shown, and malignancy does not develop. Inflammatory papillary hyperplasia may resemble mucoepidermoid tumor, for the salivary glands are involved in some cases.

- 0738 TRANSFORMATION OF FIBROBLASTS BY ALLOGENEIC AND XENOGENIC TRANSPLANTS OF DEMINERALIZED TOOTH AND BONE. (E.) Huggins, C. (Ben May Lab. Cancer Res., U. Chicago, Ill.), S. Wiseman and A. H. Reddi. *J Exp Med* 132(6):1250-1258, 1970.

Demineralized tooth and bone powder was implanted s.c. in guinea pigs, female mice, or rats to study the transformation of host tissue caused by the xenogenic implants. Osteogenesis was demonstrated by histologic study and by detection of alkaline phosphatase in transplants. Rats given 10-15 mg of coarse tooth or bone powder (from rat) developed hard calcified conglomerates of 60-150 mg 1-3 wk; alkaline phosphatase content in the transplant increased steadily for 2 wk after implantation. Implanted demineralized dentin produced cartilage in rats after 6 days, and bone after 10 days. Cartilage and bone were not observed in guinea pig connection with any of the transplants studied except with osteogenic epithelia. Demineralized mouse dentin produced large amounts of bone and cartilage in mice whereas rat dentin produced these elements in only small amounts. However, dentin produced large amounts of bone in rat host.

- 0739 STUDIES ON ENZYMES OF GLYCOLYSIS AND THE GLUCOSE SHUNT IN PRECANCEROUS RAT LIVER IN HEPATOMAS. (Ger.) Sydow, G. (German Acad. Sci. Berlin,). *Arch Geschwulstforsch* 35(4):379-383, 1970.

Enzymes participating in glycolysis were investigated in the precancerous rat liver. These included aldolase, pyruvate kinase, lactate dehydrogenase, glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase; these enzyme activities were determined in precancerous and in normal livers, as well as in primary and transplanted hepatomas. No significant differences in enzyme activities were observed between normal precancerous livers. A decrease in lactate dehydrogenase and a marked decrease in glucose-6-phosphate dehydrogenase activities were the only two notable changes.

changes in primary hepatomas. Transplanted hepatomas, however, showed marked changes in almost all parameters, with a significant increase in pyruvate kinase activity in all tested tumors; the other enzymes varied according to the tumor line. The activity of the glycolytic enzymes does not show any correlation to the tumor growth, but may be due to the loss of a specific organ function.

0740 **INTESTINAL MUCOSAL HYPERPLASIA FOLLOWING INDUCED HYPERTHYROIDISM IN THE RAT. (E.)**

Wall, A. J. (Dept. Med. U. Chicago, Ill.), W. R. J. Middleton, A. G. E. Pearse and C. C. Booth. *Virchows Arch Zellpath* 6(2):79-87, 1970.

The histological and histochemical changes which occur in the small intestine following the induction of hyperthyroidism (thyroid powder) were observed in the rat. The weight (mg/cm) of the small intestine was heavier in the hyperthyroid animal (83.2) than in the control (61.6) with a greater increase in the mucosal component (40-56) than in the muscular layer (15-20). The mucosal protein content was increased (6.11 to 7.84 mg/cm) and both villous height and total mucosal thickness were increased in the jejunum while only villous height was increased in the ileum. Height of the microvilli of the jejunal surface epithelium increased by 30% in the hyperthyroid animals. Enzyme changes were found chiefly at the brush border of the jejunal epithelium with an increase of acid phosphatase, ATP-ase, and thiamine pyrophosphatase in all 8 animals studied. Monamine oxidase activity was moderately reduced in the jejunum, ileum, and liver of the hyperthyroid rat.

0741 **CARCINOMA ON THE SITE OF COMPENSATORY HYPERPLASIA IN ADRENAL CORTEX REGENERATION.**

(Ger.) Rückert, U. (Surg. U. Heidelberg, Germany). *Chirurg* 41(9):417-419, 1970.

The underlying pathoanatomical changes in the adrenal glands leading to Cushing's syndrome, is most frequently due to a bilateral hyperplasia, which stems from a basophilic adenoma of the anterior pituitary gland. The adrenocortical carcinomas may have properties of various grades of malignancy and cell differentiation. A case is presented of a 15-yr-old boy in whom Cushing's disease developed from a bilateral hyperplasia of the adrenal cortex which was diffuse and micronodular. After subtotal bilateral adrenalectomy, there was a temporary remission under hydrocortisone replacement therapy. The remission lasted for two years after which the 17-hydroxycorticoid excretion increased to 14.0 mg/24 hr and 17-ketosteroids increased to 18.6 mg/24 hr during the subsequent 3 yr, although the therapy was discontinued. At this time surgical intervention revealed a differentiated carcinoma at the site of the subtotally resected gland. The postoperative recovery, with hormonal replacement therapy, was uneventful, but the patient died 6 months later from acute myocardial failure. Malignant degeneration in benign hyperplasia of the adrenal cortex could be avoided by bilateral total adrenalectomy.

0742 **STUDY ON THE PATHOGENESIS OF CERVICAL POLYPS. (Sp.)** Nogales Fernandez, F. (Fac. Med. Madrid, Spain) and A. Tarancon Martinez. *Acta Gynec* 21(9):659-674, 1970.

Biopsies performed on 41,000 gynecological cases (at the Dept. of Gynecology of Madrid Univ., records from January 1970) revealed 1,901 (4.6%) cervical polyps. Of these, 581 (31%) surgical samples were compared with the functional condition of the endometrium in an attempt to explore the etiological factors contributing to the occurrence of these tumors. The surgical samples revealed 44 (7.6%) proliferative normal endometria, 119 (20.5%) normal secretory endometria, 47 (8.1%) endometria with progestational insufficiency, 317 (54.6%) diffuse or cystic hyperplastic endometria, and 54 (9.3%) atrophic endometria. The high correlation between cervical polyps and glandular endometrial hyperplasia associated with progestational insufficiency (total of 63%), and the maximal age incidence between 35-56 yr suggested that hyperestrinism could be among the leading factors in the etiology of these tumors.

0743 **ENDOMETRIAL HYPERPLASIA IN YOUNG WOMEN. (E.)** Chamlian, D. L. (Armed Forces Inst. Path., Washington, D.C.) and H. B. Taylor. *Obstet Gynec* 36(5):659-666, 1970.

The pathology of endometrial hyperplasia was studied in 97 women under 36 yr old. In 24 cases, hyperplasia involved sclerocystic ovaries, an association consistent with the Stein-Leventhal syndrome. In 14 patients, initial endometrial hyperplasia progressed to adenocarcinoma in 1-14 yr after the original diagnosis; and absence of corpora lutea and albicantia were among the salient findings in these patients. In all 97 cases fertility was low, and only 26 patients conceived in the years after endometrial hyperplasia was diagnosed; only 20 of the patients who conceived carried their pregnancies to term. Thirty-seven patients continued to have menstrual irregularities from 1-30 yr after endometrial hyperplasia was diagnosed.

0744 **CERVICAL CYTOLOGY IN THE TEEN-AGE PATIENT. (E.)** Kaufman, R. H. (Baylor Coll. Med., Houston, Texas), R. E. Burmeister and H. J. Spjut. *Amer J Obstet Gynec* 108(4):515-519, 1970.

Cytological evidence of carcinoma was studied in cervicovaginal smears prepared from 10,246 women under 20 yr-of-age. Moderate dysplasia was diagnosed in 175 cases, squamous cell carcinoma *in situ* in 13; severe dysplasia was indicated in 45 smears. These findings imply that 23 of 1000 patients screened had significant dysplasia in their smears. Where conization biopsy was performed on patients in follow-up examinations (17 cases), carcinoma *in situ* was found in 4 instances, severe dysplasia in 11. In the cases of 76 patients, of whom 10 had manifested severe dysplasia, 2 follow-up smears taken after the initial diagnosis of abnormality were aberration-negative. The patients studied

were from indigent backgrounds, and 75% of them were obstetrics cases, facts which suggest that the high incidence of cervical atypia in the population studied were related to the known association of cervical carcinoma with early onset of coitus and low socioeconomic status.

- 0745 SPONTANEOUS *IN VITRO* NEOPLASTIC TRANSFORMATION OF ADULT HUMAN PROSTATIC EPITHELIUM. (E.) Fraley, E. E. (Dept. Surg., U. Minnesota, Minneapolis), S. Ecker and M. M. Vincent. *Science* 170(3957):540-542, 1970.

Studies with explants from a benign prostatic adenoma from a human patient that have had an unusually long life *in vitro*, having undergone more than 200 passages for 4 yr, are reported. The prostate gland from which the cell line was derived exhibited marked glandular hyperplasia with some areas of squamous metaplasia; however, no malignancy could be demonstrated. Cell suspension from various passages of the cell line caused solid tumors when injected into the cheek pouches of newborn hamsters which had been exposed to whole-body irradiation; tumors were composed of anaplastic epithelioid cells, and invaded surrounding connective tissue, although distant metastases did not occur. Neither mycoplasma nor viruses have been detected in cultures of the prostate cell line. This spontaneous transformation noted in cells from a benign prostatic adenoma indicate that such tissues may be pre-malignant.

- 0746 EMBRYONAL ADENOCARCINOMA IN THE PREPUBERTAL TESTIS: A CLINICOPATHOLOGIC STUDY OF 18 CASES. (E.) Young, P. G. (St. Joseph's Hosp. Lexington, Kentucky), B. M. Mount, F. W. Foote, Jr. and W. F. Whitmore. *Cancer* 26(5):1065-1075, 1970.

The treatment and histogenesis of embryonal adenocarcinoma were examined with a review of the clinicopathologic findings in 18 afflicted children. The most suggestive clinical sign was a firm non-tender testicular mass (2-12 cm) and was initially detected by the mother in 14 of the cases (78% of the cases occurred in infants under 2 years of age). Two cases in this study demonstrated that the tumor may occur in the infant and prepubertal child testis in association with teratomatous growth (previously recorded only in adult cases). The small number of cases reviewed prohibits assessment of the factors influencing survival but clinical Stage A lesions subjected to lymphadenectomy had a 75% survival rate compared to 83% without node dissection, and a Stage C case in which radical surgery was performed suggested a potential favorable effect on prognosis in selected cases. All retroperitoneal lymph nodes were negative in State A cases subjected to lymphadenectomy so that retroperitoneal lymph node dissection or irradiation may be replaced with chemotherapy. Embryonal adenocarcinoma is a testicular tumor of primordial germ cell origin which differs from the

adult embryonal carcinoma in its appearance and behavior although the histogenesis may be the same.

- 0747 PRE-MENOPAUSAL CANCER OF THE ENDOMETRIUM: SPECIFIC CLINICAL FEATURES. (Fr.) Gelle, (Hosp. Ctr. Roubaix, France), G. Crepin, M. Verhaeghe, M. F. D. Nicolle and A. Demaille. *Lille Med* 15(6):911-916, 1970.

- 0748 CLINICAL AND EVOLUTIVE ASPECTS OF THE INITIAL PHASES OF HODGKIN'S DISEASE IN RELATION TO ITS HISTOPATHOLOGICAL CHARACTERISTICS. (Sp.) Domingo, Albos, A. (2nd Dept. Path. Clin. Med., Barcelona, Spain), N. Pujol Moix, J. Sans-Sabraf, F. Ciscar Rius, J. Domingo Gomez and V. Romagosa Puig. *Rev Clin Espagn* 118(1):13-18, 1970.

- 0749 MALIGNANT MELANOMA OF THE CONJUNCTIVA. (E.) Chopdar, A. (West of England Eye Infirmary, Exeter). *Brit J Ophthalmol* 54(9):631-634, 1970.

See also:

- * (Rev): 0371, 0373, 0374, 0379, 0393
- * (Chem): 0395, 0443, 0477, 0488, 0490, 0504
- * (Phys): 0525, 0530, 0543, 0544
- * (Viral): 0560, 0599, 0672
- * (Epid-Biom): 0763
- * (Misc): 0778, 0821, 0823

0750 EPIDEMIOLOGY AND DETECTION OF BRONCHIAL CARCINOMA. (Ger.) Trendelenburg, F. (Med. J. Clin. Homburg, Germany) and W. Mall. *Internist* 11(9):303-317, 1970.

Bronchial carcinoma occurs most frequently in industrial cities and has the worst prognosis among carcinomas. The 5-yr life expectancy among all the bronchial carcinomas is between 5 and 16-17%, depending upon the time of discovery, the localization, treatment (operability) and malignancy. Operability is very much dependent upon the localization (peripheral or central), but the methods for tracing the focal area are not yet satisfactory. The intensity of the exposure of the lungs to contaminants is a major factor in the formation of carcinoma, and inhalation of smoke has been shown to be noxious, particularly cigarette smoking. Other noxious substances to which people are exposed are arsenic (formerly used in insecticides), asbestos (in the construction industry), chromium (in alloys and dyes), nickel (in alloys and dyes), isopropyl alcohol (poison gas) and by-products of coal combustion. The detection of exfoliation of the malignant cells in bronchial secretion and radiological detection provide the earliest diagnosis of bronchial carcinoma. A questionnaire regarding smoking, including questions related to possible malignancy, is presented.

0751 SCREENING FOR LUNG CANCER HIGH-RISK GROUPS. (E.) Kubik, A. (Tuberc. Respiratory Dis. Res. Inst. Prague, Czechoslovakia). *Brit Med J* 2(5710):666, 1970.

Patient interviews concerning smoking habits, cough, expectoration of sputum, blood spitting and respiratory infections were conducted on male patients aged 40-64 in an attempt to identify high-risk lung cancer groups in the Kolin district, Czechoslovakia. Information on lung cancer incidence subsequent to the interviews was obtained from notification cards, death certificates and chest clinic and hospital records. The group interviewed included 52% cigarette smokers, and 61 subsequently proven lung cancer cases (an incidence of 1.41/1000/yr.) In the group of 2707 smokers who had smoked 200,000 cigarettes and over there was a 4.64/1000 annual incidence of lung cancer; in the group of 3627 smokers who had smoked less than 200,000 cigarettes, and in the group of 1487 cigarette ex-smokers, the annual incidence was 0.87, and 0.96/1000, resp. The risk for nonsmokers was less than 0.07/1000. Persons with a chronic cough were at a 5 times greater risk than non-coughers. The annual incidence of lung cancer for men with a history of sputum expectoration was 3.30/1000, and 4.39/1000 for those with worsening coughs, and 10.20/1000 for those reporting hemoptysis.

0752 OSTEOGENIC SARCOMA. (E.) Potdar, G. G. (Tata Mem. Hosp., Bombay, India). *J Postgrad Med* 16(3):142-148, 1970.

The incidence and pathology of osteogenic sarcomas were investigated in a series of 169 cases. Tumors were most frequently located around the knee joint, with the maxilla and humerus being affected in 24 cases. The average age of patients was 19.8 yr, osteogenic sarcoma being generally more common in the second decade of life than at any other time. Males were affected more often than females (104 to 65). Only 1 case in the series showed sarcoma associated with Paget's disease and in no case was there any history of radiation therapy; however, in 48 cases there was history of trauma occurring prior to the onset of symptoms. Lungs were the most frequent site of metastasis (92 cases), with skeletal and lymph node metastasis occurring less commonly. Tumors involved the bone metaphysis and adjoining portion of the diaphysis only, with the epiphysis affected only in the later stages of the disease. Microscopically, the tumors showed variable preponderance of fibrous, cartilaginous or osteoid tissue; all tumor cells formed new bone. Surgery was the treatment of choice for osteogenic sarcoma in this series; pulmonary metastasis was common following surgery or radiation therapy. (5 references).

0753 HYDATIDIFORM MOLE, INVASIVE MOLE AND CHORIOCARCINOMA IN SWEDEN 1958-1965. (E.) Ringertz, N. (Karolinska Inst., Stockholm, Sweden). *Acta Obstet Gynec Scand* 49(2):195-203, 1970.

A review was conducted of the occurrence of hydatidiform mole, invasive mole, and choriocarcinoma in Sweden from 1958-1965, which emphasized the pathology and frequency of these conditions. The case material included 631 cases of hydatidiform mole not followed by malignancy, 13 cases of invasive mole, 10 cases of choriocarcinoma following hydatidiform mole, and 14 cases of choriocarcinoma without preceding mole. Frequencies for these conditions were calculated on the number of pregnancies in Sweden during the test period. Hydatidiform mole occurred with a frequency of 1:1,560 pregnancies; invasive mole with a frequency of 1:77,000; and choriocarcinoma with a frequency of 1:41,000. In the case of both benign mole and malignant conditions, frequencies rise significantly in women at the age of 40 yr. Women who had been pregnant 3 or more times had a higher incidence of choriocarcinoma without associated mole (43%), while women with a single pregnancy had a higher incidence of mole followed by malignancy (30%). Invasive mole was defined as having villous structures within myometrial vessels. Choriocarcinoma was diagnosed only in cases showing clearly destructive myometrial invasion by chorionic elements in the absence of villous structures. The clinical course of invasive mole cases included lung metastases in 3 cases; choriocarcinoma metastasized to the lung in 13 of 24 cases, and vaginal metastases were recorded in 2 choriocarcinoma patients. Survival data indicated that all patients with invasive mole continued to live symptom-free, while 17 of 24 choriocarcinoma patients died within 5 yr.

- 0754 MALIGNANCY AND RECORDS OF CANCER PATIENTS
IN THE PROVINCE OF KURGAN. (Rus.)
Goldberg, B. I. (Reg. Oncol. Dispen., Kurgan, USSR).
Vop Onkol 16(8):76-80, 1970.

The cancer incidence in the province of Kurgan was 181 per 100,000 population according to the 1962-1966 records. Of 5435 malignancies in males 27% gastric, 20% pulmonary, 12% lip, 9% skin and 3% bladder cancers were reported; in females 25% gastric, 20% cervical, 12% skin, 6% mammary gland and 4% lung cancer had occurred. The highest incidence of cancer occurred at the age 50-59 yr, and 88% of the malignancies occurred above the age of 40. Female susceptibility to cancer was higher than males from 5-40 yr-of-age, equal to that of males at 40-49 yr and lower than males above the age of 49 yr. In the total population of the U.S.S.R., the cancer incidence in males was 70 gastric, 53 pulmonary, 30 lip, 22 skin, 7 esophagus, and 7 bladder malignancies/100,000 population; in females 43 gastric, 37 cervical, 21 skin, 11 breast, 7 pulmonary, and 5 hepatobiliary malignancies/100,000 population were recorded. Of all malignancies 1.6% occurred in children, the incidence for age 0-19 yr being 8/100,000.

- 0755 CANCER IN CHILDREN. (Fr.) Jeliu, G. (Fac.
Med. U. Montreal, Quebec, Canada). *Un
Med Canada* 99(11):2054-2057, 1970.

According to the records of the federal statistics bureau 25,432 patients died of cancer in Canada in 1963, of which 603 (2.1%) were children 1-19 yr-of-age. Cancer occupied the 2nd place (after accidents) among the main causes of child mortality. This figure was much higher in 1967 in Quebec (2.7% for the same age group) than throughout Canada. Leukemia was the most frequent (35-50%) among childhood malignancies while brain cancer incidence was highest among the solid tumors. Neuroblastoma, Wilms' tumor, soft tissue sarcoma, osteosarcoma, and lymphomas constituted 5-10% each. The major types of cancers found in children differed from those found in adults in whom epithelial malignancies were predominant.

- 0756 HODGKIN'S DISEASE IN THE FIRST DECADE OF
LIFE. (E.) Rappaport, H. (Pritzker Sch.
Med., U. Chicago, Ill.) and S. B. Strum. *Pediatrics*
46(5):748-759, 1970.

A study of 35 case reports of children with Hodgkin's disease showed that all were more than 3 yr-of-age, and the longest survival periods were 9 and 9.8 yr. Ninety-one percent of the patients were males, 94% were Caucasian and 6% (2 patients) were Black. In 30 of 31 classifiable cases, the histologic sections showed either nodular sclerosing Hodgkin's disease or Hodgkin's disease with lymphocytic predominance. Regardless of classification, a striking preponderance of mature lymphocytes in tissue sections and a scarcity of Sternberg-Reed cells were evident in most cases. The hypothesis that a particular host response characterizes Hodgkin's disease in the young is suggested by these findings.

- 0757 FREQUENCY AND AGE DISTRIBUTION OF EPSTEIN-BARR VIRUS ANTIBODIES IN FRANCE. A PRELIMINARY EPIDEMIOLOGICAL INVESTIGATION. (Fr.)
Sohier, R. (Natl. Inst. Sanit., Med. Res., Lyon, France). *Path Biol* 18(15-18):707-711, 1970.

Indirect immunofluorescence tests were performed on the sera of 279 patients hospitalized for various conditions in order to detect and titrate antibodies to the Epstein-Barr virus. The percentage of positive reactions (> 10) in relation to age suggested that between 7 and 12 months of age, 12.5% of children had acquired antibodies, and between 12 and 24 months 47.9% had acquired antibodies. The percentages increased progressively to reach between 75% and 88% between the ages of 11 and 69 years, except for the 31-40 age group which is being investigated further. Beyond the age of 60 years 92% of the reactions were positive. Antibody titer equal to or greater than 160 found in the 12.5% sera examined and in 19.5% of the positive reactions might have been due to recent infections (e.g. infectious mononucleosis).

- 0758 AN EPIDEMIOLOGICAL STUDY OF THE EPSTEIN-BARR HERPES VIRUS IN FRANCE: FREQUENCY AND AGE DISTRIBUTION OF ANTIBODIES IN THE REGION OF PARIS. (Fr.) Chuat, J. C. (Hosp. St. Louis, Paris, France), F. Lasquelle and M. Boiron. *Path Biol* 18(15-18):713-717, 1970.

Serum samples were taken from 533 children and adults in Paris between 1965-1968, and indirect immunofluorescence tests were performed on them to detect antibodies to the Epstein-Barr virus. Antibodies were found in 50% of the children by the age of 5 yr and the proportion of reactive sera rose to 2/3 in 15 yr old children. The antibody titer was determined in 168 of the sera and was generally found higher in the youngest (1-5 yr) and during the acute stage of infectious mononucleosis. A stable titer of Epstein-Barr virus antibodies was found in individuals whose sera were titrated at yearly intervals. The high incidence of high titers of Epstein-Barr virus antibodies in children below 10 yr-of-age seemed to indicate that some viral infection occurred during childhood which bore no strict relationship to infectious mononucleosis.

- 0759 POLYPS AND CARCINOMA OF THE LARGE BOWEL IN THE SOUTH AFRICAN BANTU. (E.) Bremner, G. (Baragwanath Hosp., Johannesburg, Union of South Africa) and L. V. Ackerman. *Cancer* 26(5):991-995, 1970.

The incidence of carcinoma of the large bowel and neoplastic polyps of the bowel was investigated in the Bantu population in South Africa. In this population, cancer of the large bowel was extremely rare, only 45 cases having been admitted to this African hospital in the 12-yr study period (the hospital admitted 77,997 patients in 1967-68). Adenomatous polyps were also rare, a series of 96 patients showing no instance of polyps, and a review of 14,000 autopsies revealing no mention of

adenomatous polyps. This low incidence of cancer of the large bowel is probably an environmental feature rather than a genetic trait; in contrast to the United States (which has the highest rate of cancer of the large bowel on record) the Bantu of South Africa has an extremely bulky diet. The Bantu diet depends on maize, of which the annual consumption averages 839 l. Associated with this diet is an increased frequency of defecation with the mean time of transversal of the digesta about 3 times faster in the Bantu than in whites. The bulk of the Bantu diet and the frequency of defecation may account for the low incidence of carcinoma of the large bowel and of adenomatous polyps in these people.

0760 INCIDENCE OF MALIGNANT NEOPLASMS IN FAMILIES OF PATIENTS WITH ESOPHAGEAL CANCER. (Rus.) Satpayeva, R. A. (Kazach Res. Inst. Oncol and Radiol., Alma-Ata, USSR), and G. V. Tarasova. *Vop Onkol* 16(6):3-6, 1970.

Eighty nine cases of cancer (80 of which were cancer of the esophagus) were found in the genealogy of 75 families of esophageal cancer patients. Sixty-five (81%) of these esophageal cancers occurred in direct relatives (mother, father, son, daughter, grandparents, nephews); esophageal cancer occurred in 15 husbands or wives of such patients. Among the relatives of a group of 425 patients from Kazakhstan 70 (16.5%) exhibited esophageal cancer; of the relatives of a control group of 877 subjects 75 (8.5%) were cancer patients with only 2 cases (0.2%) of familial cancer. The incidence of esophageal cancer in the families of esophageal cancer patients from the Gur'yevsk region was 42.5% and 21.6% among the control group (9 times higher than in other regions of Kazakhstan). There seemed to be an inherited predisposition towards esophageal cancer possibly due to food habits and specific way of life.

0761 GEOGRAPHIC AND SECULAR VARIATION IN MORTALITY FROM MALIGNANT DISEASE IN OKLAHOMA: 1956-1965. (E.) Assal, N. R. (U. Oklahoma Sch. Hlth., Oklahoma City) and R. D. Lindeman. *J Okla-homa St Med Ass* 63(10):469-480, 1970.

An epidemiological study of deaths from cancer of the hematopoietic system in Oklahoma from 1956-1965 was conducted. The most common hematopoietic malignancies recorded were leukemia (accounting for 1057 deaths among white males) and lymphosarcoma-reticulosarcoma (accounting for 421 deaths among white males.) Deaths from multiple myeloma had increased during the period studied (death rates increasing from 7.1 in 1956-1960 to 10.1/100,000 in 1961-1965); other malignancies showed no increase in frequency of death rates. The average age-specific death rates for all conditions showed increases with age, and there was an early peak in leukemia deaths in the under-5-yr age group. Death rates were higher for whites in all disease categories than for non-whites. Although death rates for leukemia in white males showed no correlation with

degree of urbanization of residence, death rates for white females from leukemia were higher for metropolitan residents (death rates of 6.7 and 5.9/100,000 for "metropolitan" and "non-metropolitan" residents, resp.). Leukemia deaths showed clusters in western counties of the state, while deaths from lymphoma among white females cluster in the north-east.

0762 POPULATION KINETICS OF CARCINOMA CELLS, CAPILLARY ENDOTHELIAL CELLS AND FIBROBLASTS IN A TRANSPLANTED MOUSE MAMMARY TUMOR. (E.) Tannock, I. F. (Radiobiol. Inst., TNO, Rijswijk, Netherlands). *Cancer Res* 30(10):2470-2476, 1970.

Mice received s.c. injections of 10^5 cells of mouse mammary tumors, and tumor sections were subsequently obtained and stained for the purpose of observing the kinetic parameters in populations of capillary endothelial cells, fibroblasts and parenchymal cells; parameters were estimated by thymidine labeling techniques and by autoradiography. The mean thymidine labeling index of carcinoma cells was 35%. Mitotic index, labeling index, and mean grain count per labeled cell decreased with distance of carcinoma cells from a capillary. Values for these 3 parameters decreased from 4.3, 50.0, and 40, resp., for the region near the blood vessel, to 0.6, 10.3, and 10, resp., for the region near a site of necrosis. Migration of cells from regions of rapid proliferation near blood vessels to regions of slow or nonproliferation near necrosis was observed. The median cell cycle time was 13 hr, and the growth fraction from a repeated thymidine labeling experiment was about 50%, giving a turnover time for the carcinoma cells of about 22 hr. The mean thymidine labeling indices of capillary endothelial cells and fibroblasts were 11.4 and 9.1%, resp.; the turnover times for the endothelial cells was 50-60 hr and 70-80 hr for the fibroblasts. The mean labeling index of capillary endothelial cells remained quite constant between 10 and 40 hr after a single injection of tritiated thymidine, indicating that capillary endothelial cells are not derived from a faster-proliferating precursor population. The division of endothelial cells within the capillary walls appeared to condition the extension of the capillary network in the growing tumor.

0763 CANCER CELL DISSEMINATION IN BLOOD AND METASTASIS OF WALKER'S CARCINOMA IMPLANTS. (Rus.) Sukovatykh, L. S. (Res. Inst. Oncol. BSSR Minist. Publ. Hlth., Minsk, USSR) M. Ye. Fisher, M. Yu. Makkaveyeva, S. Z. Fradkyn, A. A. Mashevskiy, B. M. El'Perin and M. P. Stankevich. *Vop Onkol* 16(6):60-63, 1970.

The dynamics of growth and development of metastases of Walker's carcinoma were studied following partial transplantation (200 mg segments) into the gastric wall of 100 Wistar male rats. The tumor diameter reached 0.6-0.7 cm at 6-7 days, 1 cm at 9 days, 2 cm at 12 days, 3 cm at 18 days and 4 cm at 24 days after transplantation. No further growth of tumor

was noticed thereafter due to partial necrosis. Initial growth occurred at muscle levels (up to the 19th day) and mucosal penetration started on the 20th day after transplantation. An enlargement of lymph nodes could be noticed along with the growth of the tumor. Hyperplasia of the paraaortal lymph nodes was observed on the 9th day, and metastases occurred on the 13th day after transplantation. Tumor nodules in the liver and metastases in the paratracheal lymph nodes appeared at 19 days and in the spleen at 20 days after transplantation. Tumor cell blood dissemination began 6 days after transplantation and tumor cell blood levels increased along with the development of metastases. The presence of tumor cells in the blood in the early stages of tumor growth seemed indicative of the generalized nature of this process and their high capacity for dissemination throughout the blood stream, which occurred prior to the development of metastases in the regional lymph nodes.

- 0764 THE HISTOPATHOLOGY OF BRONCHOGENIC CARCINOMA AND ITS RELATION TO GROWTH RATE, METASTASIS, AND PROGNOSIS. (E.) Weiss, W. (Hahnemann Med. Coll., Philadelphia, Pa.), K. R. Boucot and D. A. Cooper. *Cancer* 26(5):965-970, 1970.

The histopathology of 161 cases of proved bronchogenic carcinoma was examined by comparing the classifications assigned by a panel of 3 pathologists (using a modified World Health Organization classification) with the diagnoses of hospital pathologists. Agreement was 84% for cases classified as squamous cell carcinoma, 67% for undifferentiated carcinoma, and 78% for adenocarcinoma. Unanimity among the 3 panel pathologists occurred in only 40% of the 161 cases and was more frequent in cases where 2 or more histological sections were available for examination and where there was a lower degree of anaplasia. Although squamous cell carcinomas have a doubling time of less than 6 months and adenocarcinomas have a doubling time of more than 6 months, the 5-yr survival rates for patients with either cancer is the same (11-12%), because squamous cell carcinomas have lower metastasis rates (63%) that adenocarcinomas (100%).

- 0765 PREVENTIVE EXAMINATIONS FOR GASTRIC CARCINOMA IN GERMANY. (Ger.) Schäfer, P. K. (Steglitz Clin., Free U. Berlin, Germany), B. Mika, R. Knöchelmann, W. Bergemann and H. Oshima. *Deutsche Med J* 21(15):996-999, 1970.

- 0766 STATISTICAL REMARKS ON THE NEOPLASTIC AFFECTION IN SARDINIA THROUGHOUT 1967. (It.) Deplano, A. (Radiol. Dept., U. Caligari, Italy) and S. Loddio. *Rass Med Sarda* 73(2):129-141, 1970.

- 0767 EPIDEMIOLOGY OF CANCER IN QUEBEC. (Fr.) Phillips, A. J. (no affil). *Un Med Canada* 99(11):2030-2033, 1970.

- 0768 MALIGNANT TUMORS, IN PARTICULAR BRONCHOGENIC CARCINOMA, IN RELATION TO THE ECONOMIC CHARACTER OF THE TERRITORY. (Cz.) Vich, (Karlovy Univ., Prague, Czechoslovakia), V. Stasek, Z. Borek, N. Havrankova, V. Maly, L. Bruckner and Tomas. *Cesk Zdrav* 18(10):361-367, 1970.

See also:

- * (Rev): 0368, 0383
- * (Chem): 0492
- * (Phys): 0540
- * (Viral): 0673
- * (Misc): 0817

769 STRAIN DIFFERENCES IN RESPONSE OF THE MOUSE MAMMARY GLAND TO HORMONES *IN VITRO*. (E.) Singh, D. V. (Michigan Cancer Found., Detroit), B. DeOme and H. A. Bern. *J Nat Cancer Inst* 45(4): 67-675, 1970.

The effect of *in vivo* pretreatment with hormones on the *in vitro* lobuloalveolar development in mouse mammary glands from different strains was tested. Female mice of 7 strains were given daily s.c. injections of 1.0 µg estradiol-17β and 1 mg of progesterone for 5, 9, and 15 days, after which mammary glands were excised and cultured with estradiol, progesterone, aldosterone, prolactin, growth hormone, and insulin, 0.001, 1.0, 1.0, 5.0, 5.0 and 0.0 µg/ml, resp. After a minimum period for pretreatment, the mammary glands were cultured in media without estradiol and progesterone. The R111 and 1st mouse strains required 5 days of pretreatment *in vivo* with estradiol and progesterone to show development *in vitro*; DBA/2, C3H, and BALB/c strains required 9 days; C57BL and A strains required 15 days. A greater length of pretreatment was correlated with the absence of the inherited hormonal influence, a hypothesis which proposes that the differences in tumor incidence in mice of various strains is related to genetically determined hormonal background. The minimal hormonal requirements *in vitro* varied with different strains. A concentration of 0.1 µg aldosterone/ml of medium was adequate for all strains except the A, which needed 1.0 µg/ml. Insulin requirements ranged from 0.5-2.5 µg/ml; prolactin and growth hormone requirements ranged from 0.1-5.0 µg/ml. There was no correlation between *in vitro* requirements for lobuloalveolar differentiation and inherited hormonal influence.

770 INCREASED INCIDENCE OF SPONTANEOUS MAMMARY TUMORS IN FEMALE RATS WITH INDUCED HYPOTHALAMIC LESIONS. (E.) Welsch, C. W. (Dept. Anat., Michigan St. U., East Lansing), H. Nagasawa and J. Sites. *Cancer Res* 30(9):2310-2313, 1970.

Unilateral electrolytic lesions were placed in the median eminence of the hypothalamus of multi-gestous mammary tumor-free rats, and a sham procedure was performed on a control group, to investigate the effect of induced hypothalamic lesions on mammary tumor incidence in rats. After 25 wk the animals were killed, the number of palpable mammary tumors was determined, and blood was withdrawn for prolactin analysis by radioimmunoassay. Mammary tumor incidence and blood prolactin levels were significantly increased in median eminence-lesioned rats (12/23, 52%; 179.8 ng/ml) in contrast to the controls (4/21, 19%; 50.9 ng/ml). These results demonstrate that disruption of the final common pathway from the hypothalamus to the anterior pituitary can significantly enhance spontaneous mammary tumorigenesis in the female rat. The role of prolactin as the principal hormonal factor in mammary oncogenesis in the rat is supported by the finding of increased blood levels of prolactin in median eminence-lesioned rats.

0771 SEROLOGY IN THE STUDY OF THE RELATIONSHIP BETWEEN *S. HAEMATOBIIUM* INFESTATION AND CANCER OF THE URINARY BLADDER. (E.) Halawani, A. (Coll. Med. U. Baghdad, Iraq), M. Al-Waidh and S. M. Said. *Brit J Urol* 42(5):580-585, 1970.

The association of schistosomiasis (*Schistosoma haematobium*) and carcinoma of the urinary bladder was investigated by means of serological tests in 52 subjects with bladder cancer in an area of Iraq which is endemic for schistosomiasis. Although 40 of the patients had a history of schistosomiasis only 6 excreted *S. haematobium* ova in the urine. Complement fixation tests and circumovum precipitin tests were performed to determine the extent of the association of schistosomal infestation with cancer of the bladder. Of 52 patients, 46 showed positive complement fixation tests, while 4 were negative and 2 gave an anti-complementary reaction. Forty-four out of 45 patients of the same series were positive for the circumovum precipitin test. All the 6 patients who passed ova in their urine were positive for both serological tests. The long duration of *S. haematobium* infestation in these cases may account for the absence of ova in the urine of the majority of patients.

0772 SYMPTOMS AND PATHOLOGY OF MULTIPLE MALIGNANCIES (163 cases). (Ger.) Becker, H. (Path. Inst. U. Graz, Germany). *Med Klin* 65(41): 1775-1781, 1970.

Multiple malignancy discovered at autopsy in 132 cases (and in 31 non autopsied cases) is described. The majority of these cases comprised males and a large group of stillborn and newborn infants. The males outnumbered the females in the 45-50 yr age bracket. Malignant neoplasm was evaluated in terms of carcinoma, sarcoma, glioma, hemoblastosis and neoplastic reticulosis. The results are tabulated according to simultaneous or sequential occurrence, localization, and succession. This multiple occurrence was usually associated with paired organs, and was due either to some endogenous tissue anomaly or subsequent to some elective exogenous damage. Patients with double malignancies do not fall into any specific age group. The patient with carcinoma does not seem to be any more susceptible to a second carcinoma (after the first was treated) than is the normal population (with the exception of carcinoma of the large intestine). The incidence of a second lesion is about 1%; the lesion is usually located near and occurs within 5 yr of the primary lesion.

0773 PLASMA GROWTH HORMONE AND HYPERTROPHIC OSTEOARTHROPATHY IN CARCINOMA OF THE BRONCHUS. (E.) Dupont, B. (U. Hosp. Copenhagen, Denmark), I. Hoyer, S. Borgeskov and J. Nerup. *Acta Med Scand* 188(1-2):25-30, 1970.

A syndrome involving hypertrophic osteoarthropathy and carcinoma of the bronchus in 3 patients is reported. The patients, 2 men and 1 woman, aged 54, 67 and 69 yr, showed edema of hands and feet

and, in 1 case, signs of acromegaly. Plasma growth hormone (HGH) assays were performed under fasting conditions and during glucose tolerance tests before and after operation on the patients' lung tumors; in 2 cases HGH levels were normal both before and after surgery, and in 1 case fasting HGH levels before surgery were elevated (20 ng/ml of plasma). In this case, elevated HGH may have resulted from autonomous secretion. It did not appear likely that hypertrophic osteoarthropathy was the result of increased production of HGH. Possibly HGH or HGH-like substances were produced by malignant lung tumors in these patients.

- 0774 GONADOTROPHIN-SECRETING BRONCHIAL CARCINOMA: ABERRANT ENDOCRINE ACTIVITY OR TROPHOBLASTIC DIFFERENTIATION? (E.) Beck, J. S. (Dept. Path., U. Aberdeen, Scotland), I. B. Porteous and J. L. Ulliot. *J Path* 101(1):59-62, 1970.

Four bronchial tumors which secreted a substance with gonadotrophin activity were studied to determine whether the tumors showed evidence of trophoblastic differentiation. Tumor tissue was stained using an indirect immunofluorescent technique which reveals human placental lactogen, a reliable indicator of trophoblastic differentiation. The primary and metastatic tumors from the patients were composed primarily of large-celled anaplastic carcinoma with marked pleomorphism and numerous tumor giant cells. Immunofluorescent staining failed to show any human placental lactogen or growth hormone in any of the tumor tissues studied. The tumors apparently were demonstrating aberrant endocrine activity, inasmuch as there was no evidence of the cellular differentiation ordinarily associated with synthesis and secretion of gonadotrophic hormones.

- 0775 METABOLIC AND BIOSYNTHETIC FEATURES OF LYMPHOCYTES FROM PATIENTS WITH DIABETES MELLITUS: SIMILARITIES TO LYMPHOCYTES IN CHRONIC LYMPHOCYTIC LEUKAEMIA. (E.) Brody, J. I. (Grad. Hosp. U. Pennsylvania, Philadelphia) and K. Merlie. *Brit J Haemat* 19(2):193-201, 1970.

Glucose metabolism and DNA synthesis was investigated in lymphocytes from patients with chronic lymphocytic leukemia and diabetes mellitus. Glucose metabolism was assayed by measuring the extent of evolution of $^{14}\text{CO}_2$ and the production of radioactive glycolytic intermediates from $1\text{-}^{14}\text{C}$ -glucose in the lymphocytes; DNA synthesis was measured by observing the incorporation by the same cells of ^{14}C -thymidine. Most diabetic lymphocytes showed depressed glucose metabolism through the direct oxidative pathway, together with depressed incorporation of labeled thymidine. Normal values for $^{14}\text{CO}_2$ evolution were $9.9 \text{ nmole of } 1\text{-}^{14}\text{C}\text{-glucose} / 1.25 \times 10^7 \text{ cells} / 3 \text{ hr}$; diabetic cells in 1 representative patient showed values of $1.9 \text{ nmole of } 1\text{-}^{14}\text{C}\text{-glucose} / 1.25 \times 10^7 \text{ cells} / 3 \text{ hr}$. Normal and diabetic cell values for thymidine incorporation were 958 and 628 cpm/ 10^7 cells, resp. In leukemic cells, glucose metabolism and thymidine incorporation were similarly depressed. In all lymphocytes assayed,

a correlative and semiquantitative relationship seen between the amount of glucose passing through the hexose monophosphate shunt (which generates NADPH) and the synthesis of DNA, a process which requires NADPH for the reduction of oxyribonucleotides to deoxyribonucleotides. The normal antigenic recognition and satisfactory initiation of the immune responses, mediated by the lymphocytes, may be based on some metabolic function, which is distributed in leukemic and diabetic conditions.

- 0776 CARCINOMA OF THE OESOPHAGUS WITH TYLOSIS (E.) Harper, P. S. (Nuffield Unit Medical Genet., U. Liverpool, England), R. M. J. Harper, A. W. Howel-Evans. *Quart J Med* 39(155):317-333, 1970.

Chromosome analysis and autopsy reports were studied in members of a family in which there is a correlation between tylosis and cancer of the esophagus; of 8 tylotic members dying since 1958, were found to have died of esophageal carcinoma; only tylotic members have exhibited esophageal carcinoma. Onset of tylosis in the family was sometimes delayed until middle age; and tylotic women were at equal risk with men of developing cancer of the esophagus. The fact that no instances of carcinoma of the esophagus occurring in children of non-tylotic parents have been recorded suggests that both carcinoma and tylosis are controlled by a single gene locus. Tylotic and non-tylotic parents showed comparable fertility, and major chromosomal abnormalities were found to a tylotic subjects.

- 0777 VITILIGO AND GASTRIC CARCINOMA. (E.) Wright, P. D. (Roy. Victoria Infirmary, Newcastle, England), C. W. Venables and R. P. R. Barber. *Brit Med J* 3(5715):148, 1970.

Anemia and vitiligo in a 46-yr-old brickyard worker were associated with gastric carcinoma. The patient presented with an enlarged nodular thyroid gland and exophthalmos together with vitiligo; surgery revealed an infiltrating carcinoma of stomach involving adjacent lymph nodes. The lesion was a moderately well-differentiated adenocarcinoma penetrating the stomach wall. The occurrence of stomach cancer in this patient with vitiligo may be more than fortuitous, given the high correlation of pernicious anemia with vitiligo and the high correlation of pernicious anemia with gastric carcinoma.

- 0778 LYMPHATICS IN MALIGNANT MELANOMA. (German) Nodl, F. (Surg. Clin. U. Saarlandes, Homburg, Germany). *Arch Klin Exp Derm* 238(2):169, 1970.

In malignant melanoma the lymphatic vessels become enlarged at an early stage in the tumor formation shortly after the primary tumor has broken through the epithelial layer, and the cell-rich infiltrates, atrophies and metastases begin to form. The a

ion that melanoma contains only one type of cell has been disproved, and specific antibodies have been found only in localized malignant melanoma. The case of a 75-yr-old patient with such melanoma is presented. Melanoma cells and micrometastases were found in the lymphatic vessels. Histological examination revealed cells which were distinguishable from the primary tumors. The hydrodynamic character of the lymph stream appears to influence the spread of the melanoma cells. The examination of the lymph is thus preferable to the blood stream for the detection of metastases.

0779 *IN VITRO* INDUCTION OF GRANULOCYTE DIFFERENTIATION IN HEMATOPOIETIC CELLS FROM LEUKEMIC AND NON-LEUKEMIC PATIENTS. (E.) Paran, M. (Weizmann Inst. Sci., Rehovot, Israel), L. Sachs, Y. Barak and P. Resnitzky. *Proc Nat Acad Sci* 67(3):1542-1549, 1970.

The conditions for the induction of granulocyte colonies from normal human bone marrow by human spleen-conditioned medium and the cloning efficiency and colony size with bone marrow and peripheral blood cells from leukemic and non-leukemic patients were determined. Human spleen-conditioned medium induced colony formation (granulocyte colonies with cells ranging from myeloblasts to mature neutrophils and granulocytes) from human and rodent (mouse and rat) bone-marrow cells, although rodent spleen-conditioned medium induced colonies only with rodent bone marrow. Bone marrow from 15 normal subjects yielded a cloning efficiency of 1 colony/ 10^3 cells seeded with an average colony size of 800 cells 14 days after seeding (subjects with bone marrow containing only 1% mature granulocytes exhibited results similar to subjects with 40%). Bone marrow from patients with acute neutrophilic myeloid leukemia had cloning efficiencies 30 times higher (1 colony/30 cells) and larger colonies (4200 cells); 1 patient with eosinophilic acute myeloid leukemia had lower cloning efficiencies (1.5 colonies/2000 cells), and 2 patients with chronic myeloid leukemia had 10- to 100-fold higher cloning efficiencies than normal subjects, and 2 gave no colonies. The cloning efficiency of peripheral blood cells from patients with acute myeloid leukemia was 350 times higher and the colony size 10 times larger than that of normal subjects. Apparently, *in vivo* failure of cell differentiation (as in the acute myeloid leukemic patients) was overcome *in vitro* by the presence of an inducer in the spleen-conditioned medium.

0780 NUTRITION AND EYE CANCER IN CATTLE. (E.) Anderson, D. E. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston), L. S. Pope and D. Stephens. *J Nat Cancer Inst* 45(4):697-707, 1970.

In experiments conducted over a 20-yr period, 435 beef cattle were fed winter feed (usually consisting of cottonseed cake and oats or milo) in varying volumes, ranging from 1-2½ pounds/day in order to investigate the association between nutrition and ocular squamous-cell carcinoma. A high level of feeding compared to a low level had an important

effect on increasing lesion manifestation as well as its rate of increase with age. More animals with more advanced lesions were observed at earlier ages in the higher feeding levels than in a medium or low level. At 7-9 yr tumors had developed in 0/5, 0/10 and 2/13 cattle fed at low, medium and high volumes, resp. With the cessation of a feeding trial, the level of susceptibility decreased compared with animals remaining on trial. These decreases were more pronounced in the higher levels than in the low-feeding level. Animals fed at a high level were also heavier and larger and had a lower survival rate than those fed at a low level. The age-adjusted disposal rate for eye cancer was higher with high levels of feeding (14%) than in the low level (1.5%). Animals fed at low levels calved at a later age, and were reproductively inferior to those fed at a high level.

0781 COMPARATIVE STUDY OF RIBONUCLEOTIDE REDUCTASE ACTIVITIES IN NORMAL AND NEOPLASTIC HUMAN TISSUE. (E.) Gordon, H. L. (New England Nucl. Corp., Boston, Mass.), T. J. Bardos and J. L. Ambrus. *Res Commun Chem Path Pharmacol* 1(6):749-756, 1970.

Ribonucleotide reductase activities (method of Gordon and Fiel) were compared in cell extracts from 19 matched human neoplastic and normal tissue pairs. The tissue pairs were grouped according to the anatomical site of origin and histological type, and the neoplasms included glandular and squamous cell carcinomas, melanomas, leiomyosarcoma, rhabdomyosarcoma, and Hodgkin's disease. The ratios of specific activities (nmoles of cytidine diphosphate- $2\text{-}^{14}\text{C}$ reduced/mg protein/hr) of tumor tissue to corresponding normal tissue ranged from 1.1 to 3.2 (the ratio was 13.0 in the case of leiomyosarcoma) in 18 of the tissue pairs studied.

0782 STEROID SYNTHESIS IN A HUMAN VIRILISING ADRENAL CARCINOMA: SOME UNUSUAL FEATURES. (E.) Cameron, E. H. D. (Welsh Natl. Sch. Med., Heath, Cardiff), J. Hammerstein, D. Jones, S. Morris and K. Griffiths. *Acta Endocr* 65(1):133-147, 1970.

Steroids in a human virilising adrenal carcinoma suspected of producing large quantities of dehydroepiandrosterone (DHA) or its sulfate (DHA sulfate) were analyzed following incubation of tumor tissue slices with $1\text{-}^{14}\text{C}$ -acetate, $7\alpha\text{-}^3\text{H}$ -pregnenolone, $4\text{-}^{14}\text{C}$ -progesterone, and $4\text{-}^{14}\text{C}$ -androst-4-ene-3,17-dione by reverse radioisotope dilution techniques. The 11β -, 17α -, 21 -, and 19 -hydroxylase systems in the tumor cells were operating efficiently based on the conversion of $4\text{-}^{14}\text{C}$ -androst-4-ene-3,17-dione to its 11β -hydroxy form (55.7%) and to its 19 -hydroxy form (0.38%) and to 19 -hydroxytestosterone (0.05%), and of $4\text{-}^{14}\text{C}$ -progesterone to cortisol (23.6%) and corticosterone (5.49%). The major metabolite for both $1\text{-}^{14}\text{C}$ -acetate and $7\alpha\text{-}^3\text{H}$ -pregnenolone was DHA suggesting that the tumor secreted DHA rather than DHA sulfate. DHA- 3β -hydroxysteroid dehydrogenase/ $\Delta^5\text{-}^4$ isomerase and DHA- 3β -sulfokinase activities appeared to be low.

- 0783 REGULATION OF ACETYLCHOLINESTERASE IN NEUROBLASTOMA CELLS. (E.) Blume, A. (Nat'l. Heart Lung Inst., Nat'l. Inst. Hlth., Bethesda, Md.), F. Gilbert, S. Wilson, J. Farber, R. Rosenberg and M. Nirenberg. *Proc Nat Acad Sci* 67(2):786-792, 1970.

The activities of acetylcholinesterase (modification of the method of Reed, Goto, and Wang) and catechol-O-methyl transferase (modification of the method of Nikodejevic, Senoh, Daly, and Creveling) in mouse neuroblastoma C-1300 were investigated *in vitro*. The specific activity (nmole product/min/mg) of acetylcholinesterase (AChE) did not change during the periods of rapid cell division, but during the stationary phase of growth it increased 25-fold (7 to 150) while the amount of protein per cell doubled (0.6 to 1.2 ng). The specific activity of catechol-O-methyl transferase did not change significantly during logarithmic or stationary phases of growth. Apparently AChE activity is regulated (inversely related) by the rate of cell division (possibly dependent upon protein synthesis) in neuroblastoma.

- 0784 HISTOCHEMICAL EVALUATION OF ENZYMES IN AMELOBLASTIC TUMORS: ACANTHOMATOUS AND GRANULAR-CELL AMELOBLASTOMA. (E.) Mori, M. (Osaka U. Dent. Sch., Japan). *J Oral Surg* 28(11):825-831, 1970.

Enzyme activity was studied in various odontogenic tumors, specifically acanthomatous and granular-cell ameloblastomas. Tumor material consisted of 106 odontogenic epithelial tumors, including 102 ameloblastomas of which 19 were squamous and squamous metaplastic acanthomas and 22 were follicular tumors. No alkaline phosphatase activity was observed in acanthomatous, granular-cell ameloblastomas or common ameloblastomas. The keratinized region in acanthomatous ameloblastoma and in squamous-cell carcinoma and homologous squamous epithelium were marked by acid phosphatase activity. Excluding the keratinized sites of squamous metaplasia oxidative enzymatic patterns in tumor cells were not altered from normal. Esterase was evident in all neoplastic structures. Granular cells of ameloblastoma were characterized by high activity for acid phosphatase and β -glucuronidase, suggesting substantial lysosomal enzyme activity. Low levels of oxidative enzyme activities in granular cells were also noted. Possibly, degenerative alterations in central ameloblastic foci are responsible for the development of granular cells.

- 0785 EFFECTS OF CANCER UPON HIGH-DENSITY AND OTHER LIPOPROTEINS. (E.) Barclay, M. (Sloan-Kettering Inst. Cancer Res., Walker Lab., Rye, N. Y.), V. P. Skipski, O. Terebus-Kekish, E. M. Greene, R. J. Kaufman and C. C. Stock. *Cancer Res* 30(9):2420-2430, 1970.

The correlation between serum levels of high density lipoproteins (HDL₂ with densities less than 1.21 g/ml) and the probability of developing cancer was examined by quantitating and characterizing serum lipoprotein (quantitative ultracentrifugation and

thin layer chromatography) in normal subjects and patients with cancer. Lipoprotein quantitation (100 ml) in normal women with no family history of cancer and normal women with such histories were similar except that the latter group averaged significantly lower levels of HDL₂ (52 compared to 100) while women with primary operable breast cancer had elevated levels of very low density lipoprotein (VLDL, 103 compared to 12) and decreased levels of HDL₂ (84 compared to 120). Women with advanced operable breast cancer and with different types of cancer had elevated VLDL (103 and 84, resp.) and depressed HDL₂ (51 and 61, resp.). Normal men with family histories of cancer had higher levels of VLDL (197) and lower levels of HDL₂ (26) than men with no such histories (43 and 97, resp.); with various types of cancer also showed elevated VLDL (230) and depressed HDL₂ (23). Children with various types of cancer had lower levels of HDL₂ than normal children (65) but VLDL levels (114 and 122, resp.) were similar.

- 0786 THE GOLGI APPARATUS DURING MITOSIS IN HUMAN MELANOMA CELLS *IN VITRO*. (E.) G. G. (Temple U. Hlth. Sci. Ctr., Philadelphia) and B. R. Brinkley. *Cancer Res* 30(9):2326-2333, 1970.

A line of human melanoma cells (LeCa 19-4) was subjected to electron-microscopy to investigate ultrastructural changes affecting the Golgi apparatus of human melanoma cells *in vitro* during mitosis. In interphase, the Golgi apparatus consisted of numerous interconnected dictyosomes, each of which was composed of 4 cisternae, as a rule. Some of these cisternae had fenestrations along their lateral edges. During prophase, the membranous tubular connections between the dictyosomes were seen to break down; no fenestration of the cisternae was observed. The number and size of cisternae were reduced; the frequency of Golgi elements reached a minimum during anaphase, although some tubular and vesicular membrane elements were present at the lateral edges of single cisternae. These were considered remnants of dictyosomes. Reconstruction of dictyosomes started at the time of nuclear envelope reformation in early telophase. The increase in number of cisternae appeared to be due to apposition of smooth endoplasmic reticulum. The persistence of Golgi elements throughout mitosis was established. The presence of coated vesicles suggested that the cisternae were functional during mitosis. A relationship between Golgi elements and premelanosomes during mitosis could not be demonstrated.

- 0787 THE ZINC CONTENT OF LEUKOCYTES IN CUTANEOUS NEOPLASIA AND NON-MALIGNANT SKIN DISEASES. (Ger.) Zaun, H. (Clin. U. Saarlande Homburg, Germany) and S. Gall. *Arch Klin Exp* 238(3):285-291, 1970.

Zinc content of leukocytes was determined (semiquantitatively) in 42 patients with malignant and premalignant skin tumors and in 70 controls with

er skin conditions. A decrease of zinc content found in all patients with mycosis fungoides, external malignant neoplasia and malignant melanoma with metastases. Patients with precancerous conditions, basal cell carcinoma and acanthoma at an early stage generally exhibited normal leukocytic levels. A non-specific decrease in zinc content was noticed in some cases of nonneoplastic disorders.

8 ELEVATION OF LEUCINE AMINOPEPTIDASE IN DISSEMINATED MALIGNANT DISEASE. (E.) Phillips, R. W. (VA Hosp., Seattle, Wash.) and E. R. Child. *Cancer* 26(5):1006-1012, 1970.

The association of elevated leucine aminopeptidase activity and malignant disease was investigated in patients with malignant conditions. Leucine aminopeptidase levels were measured in serum and urine of all patients by a colorimetric method. The most consistent finding was elevation of 24-hr urine leucine aminopeptidase in patients with invasive and disseminated malignant disease. Urine leucine aminopeptidase was elevated in all 16 cases of disseminated gastrointestinal tract neoplasms (e.g., 180-1430 U/24 hr compared to normal values 50-170 U). Nineteen of 20 cases with disseminated bronchogenic carcinoma had elevated enzyme levels in the urine (e.g., 310-2650 U). All cases of disseminated cancer of the prostate and 9 cases of invasive malignancy of the genitourinary tract showed elevated leucine aminopeptidase levels. Twelve of 15 cases of various anatomic malignancies had elevated urine enzyme levels. Serum levels (versus urine levels) were consistently elevated. Seventeen patients with localized or surgically cured malignancies had normal leucine aminopeptidase values. In only 3 of 10 patients with nonmalignant disease was elevation of leucine aminopeptidase found (excluding cases of liver or pancreatic disease).

9 MICROSPECTROPHOTOMETRIC MEASUREMENTS OF DEOXYRIBONUCLEIC ACID IN HUMAN THYROID CARCINOMAS. (E.) Lindsay, S. (U. California Sch. of Med., San Francisco). *Surg Gynec Obstet* 131(5):891-913, 1970.

Microspectrophotometric methods were used to compare the nuclear DNA contents of thyroid carcinomas with those of thyroid adenomas, diffuse toxic goiters, and normal thyroids. Feulgen-stained tissue sections were prepared from tissue taken from human patients and used for microspectrophotometric histograms for analysis of DNA content. Histograms of DNA values for papillary thyroid carcinomas were significantly lower than for other tumors, primary carcinomas for DNA contents appearing at 2c or less (arbitrary units) compared with normal thyroid values tending to 4c. DNA content values for papillary carcinoma were significantly lower than values for follicular carcinomas. Papillary carcinomas showed a wide degree of aneuploidy, with hypodiploid modes evident in 3 of the 6 instances of this lesion. Microspectrophotometric measurement of DNA content may

be useful in discriminating follicular variants of papillary carcinoma from true follicular carcinoma.

0790 TRANSFER RNA SPECIES IN NORMAL AND LEUKEMIC HUMAN LYMPHOBLASTS. (E.) Gallo, R. C. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and S. Petska. *J Molec Biol* 52(2):195-219, 1970.

A study was undertaken to identify the transfer RNA's for every amino acid in human tissues. Isoaccepting species of transfer RNA of normal and leukemic human lymphoblasts were fractionated by reverse-phase partition column chromatography, and the aminoacyl-transfer RNA profile of normal and leukemic lymphoblasts were compared by co-chromatography using ^3H and ^{14}C for labels, and the acid-activating enzyme. Differences between the aminoacyl-transfer RNA profiles of normal and leukemic cells were determined by labeled amino acid reversal and acylation with heterologous enzymes. At least 56 species of transfer RNA were fractionated from normal and leukemic lymphoblasts, and in the case of most amino acids, aminoacyl-transfer RNA profiles for both normal and leukemic cells were similar if not identical. Small but significant differences in profiles of normal and leukemic cells were detected for the transfer RNA of leucine, serine, threonine and proline. Leucine transfer RNA of leukemic lymphoblasts showed a greater amount of ^3H disintegrated/min than did leucine transfer RNA of normal cells (10 and 5% disintegration for leukemic and normal cells, resp.). Similar differences were found for normal and leukemic serine. Leukemic threonine transfer RNA eluted at a higher salt concentration than normal threonine transfer RNA. More pronounced differences between normal and leukemic transfer RNA were exhibited by tyrosine and glutamine transfer RNA, the former showing an extra isoaccepting species found only in normal lymphoblast preparations.

0791 CORRELATION OF TRANSFER RNA METHYLASE ACTIVITY WITH GROWTH AND DIFFERENTIATION IN NORMAL AND NEOPLASTIC TISSUES. (E.) Riddick, D. H. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and R. C. Gallo. *Cancer Res* 30(10):2484-2492, 1970.

Nine biological systems, consisting of cultures of human and murine tissues, both normal and neoplastic, were studied to determine whether there is any correlation between RNA methylase activity and cell growth and differentiation, or neoplasia. RNA methylase activity was identical in blast cells grown in long-term tissue culture and originally derived from the peripheral blood of normal patients and from patients with various hematological cancers (RNA methylase activity values of 70 and 43 cpm/ μg protein/hr for cells harvested in logarithmic and stationary growth phases, resp., for cells of the P-3 strain). Human lymphocytes, obtained from the peripheral blood of normal donors, which were not propagated in tissue culture and not "in cycle," had low activity (19.9 cpm/ μg protein/hr). However,

after stimulation with the mitogen, phytohemagglutinin, a 3-fold induction occurred, resulting in levels comparable to those observed in the tissue culture lines. Low and similar tRNA methylase activity was observed in bone marrow from normal individuals and patients with chronic myelocytic leukemia when marrow differentials revealed equivalent levels of cellular differentiation (around 2.5 cpm/ μ g protein/hr). However, the activity was 3-fold higher in leukemic marrows when the percentage of primitive cells (myeloblasts) was greater than 40%. Although activity was higher in spleen from leukemic AKR mice compared to normal AKR mice (14 cpm/ μ g protein/hr and 140 cpm/ μ g protein/hr, resp., for normal and leukemic mice), activity was not directly correlated with growth rate since the levels were identical in different groups of AKR leukemic cells over a 10-fold difference in growth rate. The activity was similar in two histologically similar spontaneous murine mammary tumors differing in growth rate (9.2 and 7.5 cpm/ μ g protein/hr for the fast and slow-growth lines, resp.). The data suggest that increased tRNA methylase activity, possibly including qualitatively different enzymes, is characteristic of immature normal cells as well as neoplastic cells. Furthermore, once fully expressed, tRNA methylases of neoplastic cells apparently do not increase further with an increase in growth rate. The percentage of cells in cycle seems to determine the increase in tRNA methylase activity.

- 0792 RNA DEPENDENT DNA POLYMERASE OF HUMAN ACUTE LEUKAEMIC CELLS. (E.) Gallo, R. C. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), S. S. Yang, and R. C. Ting. *Nature* 228(5275): 927-929, 1970.

Nucleic acid-free preparations from lymphocytes of peripheral blood cultures from 3 patients with acute lymphoblastic leukemia and from phytohemagglutinin-stimulated lymphocyte cultures from 48 normal subjects were prepared. No RNA dependent DNA polymerase activity was detected in any of the preparations from normal lymphoblasts. Lymphoblasts from patients with acute lymphoblastic leukemia demonstrated considerable DNA polymerase activity which was dependent on the presence of all 4-deoxynucleoside triphosphates, Mg^{+2} , and rat liver RNA; 2 μ g/ml of ribonuclease inhibited the reaction by 90%. 3H -Thymidine triphosphate was incorporated into an acid-precipitable product which was completely hydrolyzed by deoxyribonuclease. The RNA dependent DNA polymerase was completely inhibited by 460 μ g/ml of N-demethylrifampicin. The finding of an RNA dependent DNA polymerase in acute lymphoblastic leukemic lymphoblasts and the absence of this activity from normal lymphoblasts is consistent with a viral etiology.

- 0793 AUTORADIOGRAPHIC STUDIES OF THE PROTEIN SYNTHESIS IN THE MAMMARY CANCER TISSUE OF MICE. (Rus.) Gabuniya, U. A. (Georgian SSR Acad. Sci., Tbilisi, USSR) and N. N. Shiukashvili. *Vop Onkol* 16(7):43-46, 1970.

The rate of protein synthesis and metabolism in mammary gland tumor tissues was studied by autoradiography in C3H tumor-bearing mice (9-10 months old) using S^{35} methionine (0.5 μ C/g body wt, i.v.). The animals were sacrificed 15, 30 min, 1, 4, 28, 96 and 144 hr after label administration. The rate of tumor parenchymal methionine incorporation reached a maximum 60 min after tracer injection, reflecting a stage of maximal protein synthesis. After the radioactivity decreased to 50% of its maximum after 80 hr and to trace levels at 144 hr after beginning of the experiment. This decrease was possibly associated with label dilutions due to cell division processes. A redistribution of label from the tumor tissue was noticed during the experiment. 90% of the label was contained within the tumor cells and 10% was distributed in the intercellular spaces during the first minutes, but this latter activity became equal to the intracellular level at the 5th hr of experimentation, increasing thereafter through the 10th hr, when only traces of label were detectable within the cell. The intracellular to extracellular substance ratio was 56/44 in stroma-free tumor tissue samples. These data seemed to suggest that the major part of tumor cell-synthesized protein was eliminated into the intercellular spaces and that only 10% of this protein was used for growth and multiplication of the tumor cells.

- 0794 AN ABNORMAL PHOSPHOGLUCOMUTASE COMPONENT IN CHRONIC LYMPHATIC LEUKAEMIA. (E.)

L. U. (Inst. Med. Microbiol., U. Aarhus, Denmark) and K. B. Jensen. *Scand J Haemat* 7(4):243-246, 1970.

Lymphocyte phosphoglucomutase isozymes were separated by electrophoresis in 13 patients (12 males and 1 female) with chronic lymphatic leukemia and more than 90% lymphocytes in the peripheral blood. In 10 male patients, 1 or 2 extra phosphoglucomutase components were discovered between the phosphoglucomutase₂ and the phosphoglucomutase₃ series of isozymes. In 3 of the patients, the abnormal isozyme found in the peripheral leucocytes was also found in the bone marrow. However, completely normal isozyme patterns were found in lymph node biopsies.

- 0795 RECURRING DIGITAL FIBROUS TUMOR OF THE FINGER: AN ELECTRON MICROSCOPIC AND VIROLOGICAL STUDY. (E.) Burry, A. F. (Roy. Brompton Hosp., Australia), J. F. R. Kerr and J. Pope. *Pathology* 2(4):287-291, 1970.

The histological appearance of a digital fibrous tumor was examined under the electron microscope. The tumor arose on the fourth finger of a 3 month old child; upon removal another similar tumor developed at the same site. Microscopically, the tumor presented the appearance of a digital fibrous tumor of the type described by Reye. The large cytoplasmic inclusions that constitute the distinctive histological feature of Reye's lesion comprised compact masses of granules and filaments.

thout a limiting membrane in the tumor examined. They closely resembled structures that have been shown to develop in the cytoplasm of cells infected with various species of viruses and that have been interpreted as virus assembly sites. However, no viral particles could be identified in the tumor and attempts to isolate viruses were unsuccessful. Crystalline bodies were frequently found in the vicinity of the granular inclusions, but their significance was not clear. The tumor was established in tissue culture, and bodies bearing a resemblance to the cytoplasmic inclusions were found in the cultures.

96 FAMILIAL LEUKEMIA: A REPORT OF 4 CASES OF ACUTE LEUKEMIA IN 4 CONSECUTIVE GENERATIONS. (E.) Ferguson, S. W. (U. Oklahoma Med. Cn., Oklahoma City) and T. N. Lynn. *Southern Med J* (11):1337-1340, 1970.

The occurrence of 4 cases of acute lymphocytic leukemia in an Oklahoma farming family was studied. The earliest case of leukemia occurred in 1942, and the most recent in 1966. The second occurred in 1946 and was a daughter of No. 1, the mother of No. 3 and the paternal grandmother of No. 4. Onset was at an earlier age in each generation, i.e., for No. 1, 41 for No. 2, 35 for No. 3, and 14 for No. 4. Each was the second eldest child in his birthship, and all were female except No. 3. Malignant tumors occurred in 6 family members, and a blood disorder of undetermined nature in another. Cytogenetic studies in 14 close relatives revealed eight hyperdiploidy in 3 persons, one of whom also showed increased chromosome breakage. The picture of familial leukemia presented by these 4 cases is apparently consistent with the possibility of vertical transmission of an infectious viral agent in familial aggregations of leukemia.

97 CHROMOSOME ABNORMALITY AND ITS SIGNIFICANCE IN HUMAN MULTIPLE MYELOMA. (E.) Itani, S. (Kyoto Hosp., Japan), T. Hoshino, S. Kawasaki and Nakayama. *Acta Haem Jap* 33(1):54-66, 1970.

Chromosome analysis (modified method of Tjio and Chang for bone marrow cells and a modified method of Moorhead for cultured peripheral blood cells) was performed on 8 patients with myeloma and on 1 patient with primary macroglobulinemia. The modal chromosome number was 46 in all cases, and in only 2 cases a small tetraploid mode was observed. Karyograms in 2 cases showed only minor aberrations, but the remaining cases demonstrated independent abnormal cell lines characterized by MG-like, Bq-, aberrant-C, and Dq-marker chromosomes (one patient with myeloma of no-anomaly type had many marker chromosomes). Associations observed between Dq+ and MG-like, Dq+ and aberrant-C, and Bq- and aberrant-C suggest that the abnormal cell lines generate new sub-clones with new marker chromosomes. Such chromosomal abnormalities may be important in the development of the abnormal cell line of the lymphoreticular system in patients with myeloma.

0798 CYTOGENETIC STUDIES IN ACUTE MYELOCYTIC LEUKEMIA WITH SPECIAL EMPHASIS ON THE OCCURRENCE OF Ph¹ CHROMOSOME. (E.) Whang-Peng, J. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), E. S. Henderson, T. Knutsen, E. J. Freireich and J. J. Gart. *Blood* 36(4):448-457, 1970.

When bone marrow and peripheral blood of 103 patients with acute myelogenous leukemia were subjected to cytogenetic studies, 73 patients were found to have a normal karyotype and 30 patients were found to be aneuploid. No unique chromosomal abnormalities were found in patients with aneuploidy except for a significantly higher incidence of G group involvement. Four cases had a history of radiation exposure; 3 of these 4 patients had a normal karyotype and one had one Ph¹ chromosome in her bone marrow cells. Another patient with no history of radiation also had one Ph¹ chromosome in his marrow cells. Reclassification of acute myelogenous leukemia patients with Ph¹ chromosomes as a rare entity of blast crisis in chronic myelogenous leukemia rather than as acute myelogenous leukemia is proposed. Two patients exhibited the 45 chromosome syndrome before the diagnosis of acute myelogenous leukemia was made. The normal and aneuploid groups had about the same median survival time and same median date from diagnosis to chromosome study; however, although 7 patients in the normal group karyotype lived for more than 26 months from the date of diagnosis, none of the aneuploid patients survived for longer than 26 months.

0799 MYELOPROLIFERATIVE DISEASE IN A CHILD WITH MONOSOMIA OF A C GROUP CHROMOSOME. (E.) Polak, J. (Fac. Med. Hradec Kralove, Czechoslovakia) and J. Zizka. *Acta Paediat Scand* 59(5):591-595, 1970.

A 4-yr-old girl presented with a myeloid leukemic reaction with nucleated red cells and atypical lymphocytes in the peripheral blood, together with hepatosplenomegaly. The disease was benign at its first stages and did not influence the normal growth and development of the patient up to the age of 4 yr. Then an acute deterioration appeared with a picture of acute erythremia and the child died with signs of panmyelophthisis. The cytogenetic examination showed monosomia of a C group chromosome in mitoses of bone marrow cells at the age of 2 years and, in addition, a ring chromosome in this group in the terminal phase. Polycythemia vera may have led to myeloproliferative disease in this case; however, neither erythrocytosis nor thrombocytosis were observed in any phase of the disease.

0800 CHROMOSOME STUDIES IN HEMATOLOGICAL DISORDERS: III. CHROMOSOME FINDINGS IN "PRE-LEUKEMIA" AND RELATED DISEASES. (E.) Sakurai, M. (Fac. Med. Kyoto U., Japan). *Acta Haemat Jap* 33(1):127-136, 1970.

Chromosomes of 18 patients with preleukemia and other related hematological disorders (leukocytosis, poly-

cythemia vera, aplastic anemia, myelofibrosis, and purpura) were analyzed (bone marrow method of Sakurai and/or peripheral blood method of Moorhead). Abnormalities were observed in 3 patients, all of whom were suffering from aplastic anemia. An XO/XY mosaicism was detected in the marrow of 2 patients and a large Y chromosome was seen in both marrow and peripheral blood cultures of the third patient, while the 3 patients who were clinically preleukemic (and subsequently developed leukemia) exhibited no chromosomal abnormalities.

- 0801 DIFFERENCES IN Rh TYPE BETWEEN AGE GROUPS OF LEUKEMIA PATIENTS. (E.) De George, F. V. (Dept. Med. Genet., U. Wisconsin, Madison). *Nature* 228(5267):168-169, 1970.

Blood type and Rh factor were determined in 374 patients with acute or chronic leukemia to investigate the correlation between blood type and Rh factor and age, sex and chronicity of the patient. No significant differences were found in the distribution of the ABO blood groups among categories of age or chronicity; however, patients with acute or chronic leukemia in the age group 0-4 yr and 51-90 yr had higher frequencies of Rh negative factors than patients between 5-50 yr (frequencies of 22.06, 25.93, and 11.30%, resp., for acute patients and 33.33, 21.11, and 10.53%, resp., for chronic patients). The same age dependent heterogeneity in Rh frequencies was observed when data were analyzed separately for men and women; however, the frequency difference among women of different ages is not statistically significant. It may be important that the 2 age groups in which Rh negativity was unusually high among patients, 0-4 and 51-90 yr, are the age groups with the highest incidence of leukemia.

- 0802 LYMPHOSARCOMA IN THE RABBIT: GENETICS AND PATHOLOGY. (E.) Fox, R. R. (Jackson Lab., Bar Harbor, Me.), H. Meier, D. D. Crary, D. D. Myers, R. F. Norberg and C. W. Laird. *J Nat Cancer Inst* 45(4):719-729, 1970.

Twenty-nine rabbits with lymphosarcoma were subjected to pathological and genetic studies with the result that lymphosarcoma appeared to be inherited as an autosomal recessive trait, the gene involved being designated *ls*. Findings were compatible with a hypothesis of genetic susceptibility to lymphosarcoma, as well as with a hypothesis of vertical transmission of a virus. Mean age at onset of the disease was 8.4 months for females and 7.8 months for males; affected rabbits usually died between the ages of 5 and 13 months. The neoplastic involvement of lymphoreticular organs and kidneys corresponded to a pattern observed in lymphosarcoma of visceral lymphosarcomatosis of cats, which has been proved unequivocally to be caused by feline leukemia virus. This similarity between rabbit and cat lymphosarcomas involved both the sites of onset and the distribution of the neoplastic lesions and the hematologic findings of a predominantly aleukemic picture. However, in rabbit lymphosarcomas, a relative increase in circulating lymphoid cells was

frequently found, including lymphocytes of both mature and atypical forms.

- 0803 FAMILIAL PHEOCHROMOCYTOMA, MEDULLARY THYROID CARCINOMA, AND PARATHYROID ADENOMA. (E.) Paloyan, E. (U. Chicago Pritzker Sch. Med. Ill.), A. Scanu, F. H. Straus, J. R. Pickleman, D. Paloyan. *JAMA* 214(8):1443-1447, 1970.

A case is presented in which a female patient, served over a period of 15 yr, developed a malignant bilateral pheochromocytoma metastasizing to the falciform ligament and to the liver, an infiltrative medullary carcinoma of the thyroid, and 3 parathyroid adenomas, 1 having an unusual vascular distribution. The patient had a sister and a brother of whom had developed bilateral pheochromocytoma. High concentrations of calcitonin in the medullary thyroid cancer (250-750 times normal calcitonin activity) was observed. Morphologically, the medullary thyroid tumor and the metastases from the pheochromocytoma were similar. In view of the recent discovery of a calcitonin-like substance in the adrenal medulla and the morphological similarity between the calcitonin-producing cancer and the pheochromocytoma's metastases, it may be that the syndrome shown by this patient represents a defect in the neuroectodermal cell system.

- 0804 CHROMOSOMAL CHARACTERISTICS OF NEUROBLASTOMAS IN CHILDREN. (E.) Mark, J. (Path., U. Lund, Sweden). *Acta Cytol* 14(8):511-514, 1970.

Chromosomes were studied in preparations from neurogenic tumors in children, the tumors examined including 3 primary and 1 metastatic medulloblastomas, 1 optical glioma and 2 primary and 1 metastatic neuroblastomas. Among the primary tumors about 75 per cent had their mode in the diploid group and in the polyploid group the tetraploids were more frequent than the triploids. The same pattern of modality occurred in primary malignant gliomas of the adult, whereas in other solid neoplasms in adults the diploids were found in a considerably lower frequency and the triploids outnumbered the tetraploids. The gliomas in adults differed from the neurogenic tumors in children by the absence of tumors with a normal, diploid stemline and few tumors with a pseudodiploid mode. The metastatic tumors also showed a higher frequency of stemline in the diploid region in comparison with corresponding lesions in the adult, but the progression trends were similar in both materials. In both primary and secondary neurogenic tumors in children structural aberrations were somewhat more frequent than in correspondent neoplastic conditions in the adult. A statistical analysis of the chromosomal representation in the tumor stemlines of the children revealed a non-random pattern; though less pronounced, the characteristics of this pattern were similar to those observed in advanced tumors in the adult. Apparently, in a given tumor group, the chromosomal characteristics are significantly related with the tissue of origin and the length of growth period.

05 CHROMOSOMAL ANALYSIS OF A HUMAN RETINOBLASTOMA. (E.) Mark, J. (Inst. Path., U. Lund, Sweden). *Acta Ophthalmol* 48(1):124-135, 1970.

errations in the chromosomes of cells taken from sporadic human retinoblastoma were studied in preparations of the tumor tissue. The karyotype of the retinoblastoma was characterized from the analysis of 51 metaphases; hyperdiploid stem-side-lines with characteristic marker chromosomes, a restricted spread around the stemline number, and the polyploid mitoses were observed. The findings differed completely from the inconsistent pattern reported for another sporadic retinoblastoma, investigated exclusively after explantation *in vitro*. This previously described retinoblastoma, a deletion affecting one of the long acrocentrics (D chromosome) was found both in normal and tumor cells. This deletion was not seen in the present case. A pattern of early and gradual substitution of tumor cells by stroma cells was observed from *in vitro* examination of this retinoblastoma. No obvious similarities were found between the chromosomes of the retinoblastoma and those of medulloblastomas or neuroblastomas.

06 Dq-, Dr AND RETINOBLASTOMA. (E.) Taylor, A. I. (Guy's Hosp. Med. Sch., London, England). *Humangenetik* 10(3):209-217, 1970.

Information on 30 cases of patients with Dq- or Dr chromosomes, 28 from the literature and 2 new reports, was assembled to survey the symptoms associated with these chromosomal abnormalities; prominent symptom associated with the condition was retinoblastoma. Both the new cases involved male infants of normal parents who presented the chromosome; 1 patient showed marked abnormalities including mental and growth retardation, while the other showed less severe abnormalities including retardation and bilateral retinoblastoma. Six of 11 Dq- patients in the case reviews had retinoblastoma, while none of the 15 Dr cases had retinoblastoma. All retinoblastoma patients showed mental and physical retardation, and most had minor somatic anomalies. The gene associated with retinoblastoma may be positioned on the proximal D arm near the centromere, a hypothesis which would explain the absence of retinoblastoma in the chromosome cases which have fairly long ring chromosomes with small long arm deletions.

07 DESULFURASE ACTIVITY AND CHROMOSOME ANALYSIS OF CULTURED RAT HEPATOMA CELLS. (E.) Jackson, J. F. (Sch. Med. U. Mississippi, Jackson) and P. A. Morse. *Europ J Clin Biol Res* 15(8):906-910, 1970.

Cysteine desulfurase and β -mercaptopyruvate desulfurase activities (modified tetrazolium method of Barrett) and chromosome modalities were determined in cultured rat hepatoma cells (Novikoff N1 and N2 and Reuber H4A and H4C). The modal chromosome number was 39 for both strains of Novikoff tumor, 55 for Reuber H4A, and 56 for Reuber H4C compared to

the normal 42 for the rat. The chromosomally heteroploid Reuber hepatomas were generally low in both cysteine and β -mercaptopyruvate desulfurase activities (85-92% of the total cells showing only faint staining), while the near diploid Novikoff hepatomas exhibited greater desulfurase activity (56-67% of the total cells showing readily detectable or heavy staining). An accumulation of β -mercaptopyruvate in tumors deficient in desulfurase activity may contribute to the development of polyploidy.

0808 FAMILIAL OVARIAN CARCINOMA. (E.) Li, F. P. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), A. H. Rapoport, J. F. Fraumeni, Jr. and R. D. Jensen. *JAMA* 214(8):1559-1561, 1970.

In a white family of Anglo-Saxon origin, ovarian carcinoma occurred in 4 sisters and in 6 of their relatives over 3 generations; the tumors were primarily papillary adenocarcinomas, a histological type reported in another case of familial ovarian cancer. In this family examined, ovarian carcinoma appeared to be transmitted through males as well as through females, and the pattern of involvement suggested the activity of a dominant gene with variable penetrance or possibly a polygenic mechanism. Familial occurrence of ovarian carcinoma may result from genetic susceptibility of ovarian tissue to hormonal or other carcinogenic influences. Alternatively, the genetic defect may induce hormonal imbalance which is potentially carcinogenic.

0809 CHROMOSOME CHANGES IN INVASIVE CARCINOMAS OF THE UTERINE CERVIX. (E.) Auersperg, N. (Cancer Res. Ctr., U. British Columbia, Vancouver, Canada) and T. Wakonig-Vaartaja. *Acta Cytol* 14(8):495-501, 1970.

Chromosome preparations from 8 cases of invasive squamous cell carcinoma of the cervix were subjected to karyotype analyses to investigate chromosome changes associated with cervical carcinogenesis. The chromosome distribution in the 8 carcinomas varied considerably between individual cases, but there was a reduced proportion of chromosomes in group B in all tumors, and in groups A, D and G in most tumors. The proportion of chromosomes in groups C and E was usually increased. Recurring markers included ring chromosomes in four of the carcinomas and an Api chromosome in an early invasive lesion. Apparently, there is a correlation between the varying stages of the disease and the nonrandom chromosomal changes which occur in cervical carcinogenesis.

0810 SEX CHROMATIN IN ENDOMETRIAL CANCER. (E.) Siracky, J. (Oncol. Inst. Bratislava, Czechoslovakia), B. Belohorsky and E. Siracka. *Neoplasma* 17(4):399-403, 1970.

The incidence and characteristics of sex chromatin material in patients with endometrial cancer was investigated. Primary tumor sections from 119 patients with endometrial cancer were examined; some

patients had been treated with surgery, and some with radiation therapy. Tumor tissue was sex chromatin-negative in 22.7% of cases, positive in 77.3% (where "sex chromatin-negative" cells contained less than 10% sex chromatin bodies in their nuclei). Most sex chromatin-negative cases (70%) appeared as poorly differentiated cancers. The total 5-yr survival rate after treatment (surgery and/or radiation) was higher in the group of sex-chromatin positive cases (sex chromatin positive cases 54%, sex chromatin negative cases 40%). In the group of sex chromatin negative cases which were given radiation therapy the 5-yr survival was 26% only, while in the group of sex chromatin positive cases having radiation therapy 5-yr survival amounted to 58%. A relationship between the biological properties of the tumor and its cytogenetic characteristics may be indicated by the observed difference in survival rates.

- 0811 SPONTANEOUS KIDNEY TUMORS IN A SUBSTRAIN OF R111/Dm/Se MICE. (It.) Ribacchi, R. (Dept. Res. Cancer, U. Perugia, Italy). *Lav. Anat. Pat. Perugia* 30(2):73-88, 1970.

The occurrence of 7 multiple nodular transplantable spontaneous kidney tumors of tubular epithelial origin was observed through 50 generations (a total of 5300 animals) of 3 substrains (A, B, C) of R111/Dm/Se inbred mice. The mice were maintained on a normal pellet diet. The first kidney tumor occurred in a male of the 40th inbred generation of the A substrain and 6 kidney tumors occurred in 5 males and 1 female (bearing a minor mammary tumor) in 3 consecutive generations of the B substrain (1 in the 43rd, 2 in the 44th and 3 in the 45th, the latter occurring in descendants of the brood in which the first tumor occurred) at 548-599 days of age. No mouse of the C substrain developed kidney tumors. The incidence of kidney tumors throughout the 3 mentioned generations in the B substrain was 50% (5 out of 10 animals) in males and 10% (1 out of 10) in females, while the other 90% of females developed mammary tumors at an average age of 455 days. The incidence of mammary gland tumors in 3 groups of generations of the B substrain (females of the 36-42nd, 43-45th and 46-49th generations) was 44% (12 out of 27), resp., and occurred at the average age of 434, 455 and 332 days, resp., indicating that a weakening of the MTV potency occurred in the generations preceding the appearance of the kidney tumors. The C breeders exhibited the highest incidence of mammary tumors (94% occurring at an average age of 266 days through the 36-49th generations), while the B breeders had the lowest incidence (69% occurring at the average age of 402 days). The development of kidney tumors seemed to be determined by chromosomal and/or extrachromosomal factors interfering with the transmission of the potency of the MTV.

- 0812 PROLIFERATION AND DIFFERENTIATION OF PIGMENT CELLS *IN VITRO*. (E.) Hu, F. (Oregon Reg. Primate Res. Ctr, Beaverton) and Y. Kitano. *J Invest Derm* 55(6):444-451, 1970.

The relation between proliferation and melanin maturation (quantitated by a modification of the method of Foster, Tremblay, and Stamas) was studied in layer cultures of mouse pigment cells. A pigmented cell (440B) proliferated to form a colony of pigmented cells (not all the colonies formed uniformly pigmented), and a nonpigmented cell formed a nonpigmented colony. The melanin content (measured by optical density) of a cell did not increase until the proliferation had decreased (2.66 at 6 days, 3.37 at 9 days, 3.37 at 12 days, and 5.40 at 15 days). Light did not significantly alter the cell count (363.8×10^4 compared to 371.7×10^4 cells at 15 days) but did lower the melanin content (2.24 compared to 3.37 at 12 days), and culturing on the edge of the dish increased the melanin content (6.08 compared to 4.08 at 15 days) without affecting cell count (280.8-324.9 cells). Radioisotope incorporation studies (^{14}C -tyrosine and ^3H -thymidine) indicated that the values of thymidine incorporation (protein synthesis) were inversely related to thymidine incorporation (melanin synthesis).

- 0813 PROLIFERATIVE ACTIVITY AND CYTOCHEMICAL PROPERTIES OF NUCLEAR CHROMATIN RELATIVE TO LOCAL CELL DENSITY OF EPITHELIAL CELLS. (E.) Terberg, A. (Karolinska Inst., Stockholm, Sweden) and G. Auer. *Exp Cell Res* 62(1):262-270, 1970.

Proliferative activity (DNA synthesis and cytochemical properties) and cytochemical properties (capacity to bind acridine orange and resistance to heat denaturation) of nuclear chromatin were studied in relation to the function of local cell density in primary monolayer cultures of mouse kidney epithelial cells. Confluent cell layers were found to occupy a constant surface area in the culture in inverse proportion to the cell density. As cell densities (cell number per unit area) increased from 10,000 to 50,000 the percentage of ^3H -thymidine-labeled cells dropped rapidly (from 5% to 1%); from 50,000 to 100,000 it decreased slowly (to 1%), and above 150,000 no further incorporation was detected, although small "non-proliferative" areas with cell densities of 250,000 were seen that might have resulted from cellular crowding or epithelial sheet retraction. Cells in these non-proliferative areas bound 40% more acridine orange than cells in the lower density areas, and the chromatin was more resistant to heat denaturation. At low cell densities (below 10,000) cell nuclei contained postmitotic, intermediate levels of DNA, but at higher densities the cell nuclei contained only postmitotic levels of DNA, indicating that the inhibition of cell proliferation resulted from the failure of the initiation of DNA synthesis in the G_1 phase.

- 0814 THE INFLUENCE OF NORMAL CELLS ON THE PROLIFERATION OF TUMOR CELLS IN CULTURE. Weiss, R. A. (Dept. Anat., Embryol., U. College London, England). *Exp Cell Res* 63(1):1-18, 1970.

The effect of population density of normal cells on the proliferation of tumor cells (chick, mouse, rat, quail, and embryo cells) on the proliferation of Rous,

sarcoma 180 cells was studied. Rous sarcoma virus (RSV)-transformed chick embryo cells proliferated without density dependence on the sparse proliferating ($375-500$ cells/mm²) and on the dense static (1500 cells/mm²) sheets of normal chick embryo, and the transformation of normal cells was inhibited at high densities. On dense sheets of chick embryo cells fully-transformed cells were inhibited but freshly infected cells were markedly stimulated (21-27 Rous foci compared to 249-276 with fully-transformed cells). RSV-transformed cells originating from chick, rat, or hamster embryos were not inhibited by dense sheets of normal mouse or chick cells; polyoma and S180 cells were inhibited on dense sheets of mouse or rat cells but not by chicken, goose, or chick cells. Both mouse and chick cells exerted a feeder effect on tumor cell growth on monolayer and suspension. Different types of tumor cells respond differently to the inhibitory influence of crowded normal cells, and avian and mammalian embryo cells exhibit different capacities to inhibit tumor cells.

5 THE SYNERGIC EFFECT OF ESTROGENS AND POLYETHYLENE STRIP INSERTIONS ON THE UTERINE TUBES OF GUINEA PIGS. (Fr.) Raitcheff, I. (Higher Inst. Med., Sofia, Bulgaria). *Bull Cancer* 67(1):121-132, 1970.

The morphological alterations of guinea pig uterus were studied after local application of vitestrol, a Bulgarian estrogenic preparation, after castration (15-20 days before treatment) and after ligation of the uterine tubes by means of polyethylene strips. Fifty-eight female guinea pigs were castrated and divided into 4 groups: one group consisted of 12 animals having the top ends of both uterine tubes ligated with 2 mm wide polyethylene strips and treated with 15,000 I.U. of vitestrol weekly for 2½-6 months; the 2nd group consisted of 22 animals with unilateral (right tube) ligation, otherwise treated identically for 3-week months with 1 animal treated for 9 months; the 3rd (10 animals) and 4th (14 animals) groups were controls subjected to bilateral and unilateral ligation and were given no vitestrol. Nodular hyperplastic proliferations of the connective tissue were noticed on the top segments of uterine tubes in 12 animals of the 1st and 17 animals of the 2nd group (receiving 105,000-555,000 I.U. of vitestrol). Neoplastic proliferation (fibroma) was observed close to the ligation sites in 5 animals of the 1st and 8 animals of the 2nd group. Irregular hyperplastic proliferation where the collagenous fibers lost their usual orientation and diffuse leiomyomatous structures were noticed in 1 animal of the 1st group after 2½ months of treatment. Hyperproliferation of the collagenous connective tissue of the ligated tube segment was noticed in 1 animal of the 2 control groups 10 months after unilateral application of the strip. No neoplastic proliferations occurred in the control animals.

6 THE TUMOR GROWTH PROMOTING EFFECT OF ε-N-TRIMETHYL LYSINE. (E.) Szende, B. (Semmelweis Med. U., Budapest, Hungary), E. Tyihak, L. Szepes and K. Lapis. *Neoplasma* 17(4):433-434, 1970.

Tumor-bearing female mice were given i.p. or s.c. doses of 5-10 mg/kg body wt of pure DL-ε-N-trimethyl lysine, and the growth-promoting effect of this compound on Ehrlich subcutaneous carcinoma and NK/Ly ascites lymphoma was observed; ε-N-methylated lysine components have previously been ascertained to be the basic protein fraction of the cells of these tumors. Tumor growth was promoted by as much as 50-60% in the 2 tumor types following treatment with the compound in doses of 5 and 10 mg. In the case of the ascites lymphoma, an i.p. 10 mg dose produced an elevated DNA level in tumor cells after 6 hr, and, after 24 hr, an elevation of the whole protein-level. Larger amounts of ε-N-methylated lysine were found in the arginine-rich histone and in the acid-insoluble protein fraction of treated tumor cells.

0817 THE EFFECT OF RNA, ISOLATED FROM BONES AND EMBRYONAL TISSUES, ON THE GROWTH OF M-1 SARCOMA. (Rus.) Pankov, E. Ya. (Serbsky Inst. Prosthet. Orthop. Traumat., Kharkov, USSR) and N. V. Dedukh. *Biull Eksp Biol Med* 70(9):72-75, 1970.

The effect of bone and embryonal tissue RNA on tumor growth was studied in 128 rats (80-90 g). Control animals were inoculated s.c. with a suspension of M-1 sarcoma cells (100% transplantability). RNA extracted from rat bones was added to tumor cell incubation media containing 800,000 cells at a ratio of 48 and 50 µg/ml. Embryonal RNA (obtained after the removal of internal organs, head and skin) was added in amounts of 50, 500 and 1000 µg/ml of nutrient media containing 800,000 cells. RNase-treated RNA and trypsin-treated RNA were added to other samples of sarcoma cell cultures. All animals were sacrificed 20 days after cell culture inoculation. Bone RNA decreased the tumor transplantability by 38-59%, but ribonuclease-treated RNA exhibited no inhibitory effect on tumor development; trypsin had no effect on the RNA-determined tumor growth inhibition. RNA from embryonal tissue produced no tumor growth inhibition effects.

0818 STIMULATION OF MITOTIC ACTIVITY IN RAT BONE MARROW AND THYMUS BY EXOGENOUS ADENOSINE 3'5'-MONOPHOSPHATE (CYCLIC AMP). (E.) Rixon, R. H. (Div. Biol., Natl. Res. Council Canada, Ottawa), J. F. Whitfield and J. P. MacManus. *Exp Cell Res* 63(1):110-116, 1970.

Mitotic activity in rat bone marrow and thymus cells was determined in the presence and absence of Colcemid (0.2 mg/100 g, i.p.) after i.p. administration of adenosine 3',5'-cyclic monophosphate (cyclic AMP), dibutyryl adenosine 3',5'-cyclic monophosphate, or AMP. The proportion of cell population which reached Colcemid-metaphase in 6 hr was increased from 14% to 18.5% by cyclic AMP (5 mg/kg, i.p.), from 5.4% to 8.0% by the dibutyryl derivative of cyclic AMP, and was not affected by AMP (2-15 mg/kg, i.p.). The stimulatory activity of these nucleotides was limited to doses between 4 and 6 mg/kg (when 15 mg/kg was tested, a 4 hr delay was observed while the mitogenically ineffective level of circulating nucleotide decreased to a stimulatory

level). The stimulatory activity of dibutyryl-cyclic AMP was also evident in the absence of Colcemid (the mitotic index increased from 1.14% to 2.17% in bone marrow cells and from 0.79% to 1.53% in thymus cells). The stimulatory ability of cyclic AMP supports the hypothesis that this cyclic nucleotide is an intracellular initiator of cell proliferation in lymphoid and hematopoietic tissue.

- 0819 *IN VITRO* DIFFERENTIATION OF A MURINE PLASMOCYTOMA REVEALING TWO PHENOTYPICALLY STABLE STAGES. (Fr.) Paraf, A. (Inst. Molec. Biol., Paris, France), M. A. Moyne, J. F. Duplan, R. Scherrer, M. Stanislawski, M. Bettane, L. Lelievre, P. Rouze and J. M. Dubert. *C R Acad Sci* 271(10):839-842, 1970.

A partially reversible phenomenon of cell differentiation characterized by two phenotypically different stages was established *in vitro* in a murine plasmacytoma. The original tumor (MOPC 173) maintained in BALB/c mice was cultivated *in vitro* on Earl's media with added yeast extract, lactalbumin, vitamins, calf serum and tris-buffered mouse embryo extract. The developed cell cultures were subjected to trypsin digestion a few weeks later and placed in similar media without embryo extract but containing 2% serum (to enhance the development of epithelial cells) or 10% serum (to favor the development of fibroblastic type cells). Two distinctive cell lines were thus obtained by differential trypsin treatment: a fibroblastic line, susceptible to trypsin hydrolysis, with oncogenic properties and containing large numbers of type A and about 1% of type C virus-like particles; and an epithelial cell line which was not susceptible to trypsin but was dissociated by EDTA and which had no oncogenic properties and contained no virus-like particles. The epithelial cells were able to become fibroblastic when transferred into media favorable for fibroblastic cell cultivation.

- 0820 BRONCHOALVEOLAR CANCER OR PULMONARY ADENOMATOSIS (JAAGSIEKTE) OF SHEEP. (E.) Enchev, S. (Vetr. Inst. Infect. Parasit. Dis., Sofia, Bulgaria). *Neoplasma* 17(4):415-425, 1970.

The lungs, pulmonary lymph nodes and viscera of 272 sheep and lambs afflicted with histologically demonstrated pulmonary adenomatosis were examined to determine if the condition is essentially neoplastic. Macroscopic features observed in pulmonary adenomatosis included intrapulmonary spreading and metastases in the lung lymph nodes in 73% and 8% of specimens. In 66% of the cases necroses were found in the lungs. Changes most often took the form of papilliferous adenoma, and usually originated in the bronchiolar epithelium. Metastatic foci showed a more malignant growth pattern, often resembling adenocarcinomas. On the basis of observed metastasis, necrosis and cellular atypism, it seems that pulmonary adenomatosis of sheep should be classed with neoplastic diseases.

- 0821 THE MODE OF SPREAD OF HODGKIN'S DISEASE TO THE SKIN. (E.) Benninghoff, D. L. (U. New York Downstate Med. Ctr., Brooklyn), A. Medina. *Cancer* 26(5):1135-1140, 1970.

Ten cases of Hodgkin's disease with definite subcutaneous involvement were reviewed to determine the mechanism of the skin invasion. The site of skin involvement among the 10 patients was random (skin or subcutaneous tissues of the head, arm, chest, and thigh), but a close relation existed between the site of initial lymph node involvement and the site of subsequent skin involvement which always occurred in the drainage area of extensively involved lymph nodes. The mechanism of skin involvement is a passive one in which the neoplastic cells are carried to the skin with a backflow of lymph resulting from a lymph node obstruction. Retrograde lymphatic spread of Hodgkin's disease constitute a major mechanism of its spread.

- 0822 METASTASIS: QUANTITATIVE ANALYSIS OF DISTRIBUTION AND FATE OF TUMOR EMBOLI LABELLED WITH ^{125}I -5-IODO-2'-DEOXYURIDINE. (E.) Fidler, J. (Sch. Dent. Med., U. Pennsylvania, Philadelphia). *J Nat Cancer Inst* 45(4):773-782, 1970.

A technique for quantitative studies of metastasis using young adult mice given i.v. injections of 10^5 pure melanoma cells grown in tissue culture and labeled with ^{125}I -5-iodo-2'-deoxyuridine is described. Mice were killed 2-3 wk after inoculation with the labeled cells, and the distribution and disposition of labeled tumor emboli were examined. Since the label was released only after cell death and was poorly reutilized and quickly eliminated, organ radioactivity represented almost exclusively the number of live cells present when the animals were killed. The lung contained most of the tumor cells in mice killed at all intervals. Some tumor cell emboli recirculated. Tumor cells in the lung decreased in numbers at about 5 min post injection. Tumor cells died rapidly, and about 1% of cells survived after 24 hr. About 400 melanoma cells were in the lung after 14 days, and those yielded an average of 78 metastases. Metastases could readily be established by a very few surviving tumor cells.

- 0823 PAPILLARY CARCINOMA OF THE THYROID: DEVELOPING PATTERN OF METASTASIS. (J) Noguchi, S. (Noguchi Thyroid Clin. Beppu, Japan), A. Noguchi and N. Murakami. *Cancer* 26(5):1051-1060, 1970.

The developing pattern of metastasis was determined by histological examination of the excised lymph nodes from 57 patients with papillary adenocarcinoma of the thyroid (metastasis was evident in 90% of these cases). A majority of the metastases (57%) were small (less than 3 mm in diameter); there was a correlation between the size of the primary tumor and the number of metastases, but no relation between the localization of primary tumors and the

nce or distribution of metastases was suggested. The sequence of metastatic concentration was pretracheal and paratracheal nodes, deep lower and lateral, and deep upper submandibular nodes for patients with small numbers of metastases, and pretracheal and paratracheal, paraglandular and deep per cervical, deep lower and lateral cervical, and submandibular nodes for patients with more extensive metastases. The paratracheal nodes appear to be most susceptible to metastasis of papillary thyroid carcinoma, regardless of the location of the primary tumor.

- 24 TUMOR GROWTH INHIBITING EFFECT OF JB-1 ASCITIC FLUID: I. AN *IN VIVO* INVESTIGATION (E.) Bichel, P. (Cancer Res. Inst., Aarhus, Denmark). *Europ J Cancer* 6(9):291-296, 1970.

mitotic indices and growth rates of a transplantable ascitic tumor (JB-1) were determined in mice after removing the ascitic fluid and replacing it with fresh cell-free tumor ascites or with "normal ascites" from non-tumorous mice. Three days after inoculation of the tumor the mitotic index peaked at 3-4%, then dropped off to 1.5% on day 5 or 6, and decreased slowly until the death of the animal. Aspiration of the tumor on day 10 followed by injection of tumor ascites or normal fluid twice daily raised the index to 3% from which it again decreased. Methylcine treatment on the second day after aspiration revealed more tumor cells in metaphase in mice subjected to total aspiration (5%) and in those receiving "normal ascites" after aspiration (6.5%) than in mice receiving tumor ascites after aspiration (2%) or in controls (1%). When tumor ascitic fluid was injected for only 2 days after aspiration, the mitotic index increased after discontinuation of the injections (to 2.2%), indicating that the tumor cells were capable of resuming accelerated growth. Inhibition of recurrent growth following daily injections of tumor ascites suggests that a humoral mitotic factor might be involved in the growth regulation of this tumor system.

- 25 CARCINOMA OF THE COLON FOLLOWING URETERO-SIGMOIDOSTOMY: REPORT OF A CASE. (E.) Stjten, L. H., Jr. (Orlando, Florida), J. L. Campbell, M. W. Thomley and R. L. Parsons. *J Urol* 104(4):536-537, 1970.

- 26 SOME CONSIDERATIONS ABOUT TWIN ZYGOSITY AND CONCORDANCE DETERMINATION IN CANCER RESEARCH. (E.) Martynova, R. P. (USSR Acad. Sci., Novosibirsk). *Acta Genet Med Gemellol* 19(1-2):65, 1970.

- 0827 POLYPOID LYMPHOID HYPERPLASIA OF THE TERMINAL ILEUM IN PATIENTS WITH FAMILIAL POLYPOSIS COLI AND WITH GARDNER'S SYNDROME. (E.) Vanhoutte, J. J. (U. Colorado Med. Ctr., Denver). *Amer J Roentgen* 110(2):340-342, 1970.

- 0828 PHEOCHROMOCYTOMA ASSOCIATED WITH VON HIPPEL-LINDAU'S DISEASE IN A FAMILY. (E.) Sander, S. (U. Hosp. Oslo, Norway), T. Norman and W. Mathisen. *Scand J Urol Nephrol* 4(3):259-263, 1970.

- 0829 HISTOLOGY AND CYTOMORPHOLOGY OF LUNG CANCER. (Ger.) Fasske, E. (Res. Inst. Borstel, Germany). *Internist* 11(9):318-327, 1970.

- 0830 HEREDITARY SKIN MELANOMA: TWO CASE REPORTS. (Rus.) Nivinskaya, M. M. (Acad. Med. Sci. USSR, Moscow) and L. R. Paches. *Vop Onkol* 16(8):81-83, 1970.

RONSON, S.A.
 0557, 0589, 0638,
 0659, 0668
 ELEV, G.I.
 0596, 0598
 HONG, B.G.
 0619
 KERMAN, L.V.
 0759
 AM, E.
 0624
 AM, M.
 0719
 EKUNLE, A.A.
 0425
 ENIS, L.
 0493, 0494
 ARWAL, S.S.
 0703
 EENKO, A.I.
 0618
 EXANDER, P.
 0725
 -FALLUJI, M.M.
 0682
 LEN, D.W.
 0582
 LIETTA, M.
 0682
 VAREZ, Y.
 0554
 -WAIDH, M.
 0771
 BRUS, J.L.
 0601, 0781
 DERSON, D.E.
 0780
 DREWS, P.
 0508
 GULO, M.
 0502
 ONYMOUS
 0349, 0352, 0367,
 0372, 0375, 0376,
 0687, 0688.
 THONY, P.P.
 0723
 OSHIAN, H.V.
 0674, 0683
 AI, Y.
 0416
 COS, J.C.
 0466, 0474
 GUS, M.F.
 0466, 0474
 NOLD, H.P.
 0427
 ON, M.
 0731
 THUR, E.
 0565
 SAL, N.R.
 0761
 BERT, C.
 0444
 BERTIN, A.M.
 0522
 ER, G.
 0813
 ERSBERG, N.
 0809

AUTHOR INDEX

AURELIAN, L.
 0623
 AURICH, G.
 0712
 BABAKOVA, S.B.
 0616
 BABKOVA, O.V.
 0654
 BADER, A.V.
 0566
 BADER, J.P.
 0566
 BAEYENS, W.
 0544
 BALDWIN, R.W.
 0361
 BALFOUR, I.C.
 0714
 BALKUS, M.
 0421
 BALL, R.A.
 0403
 BALLS, M.
 0565
 BALNER, H.
 0357
 BANATVALA, J.E.
 0353
 BARAK, Y.
 0779
 BARANSKA, W.
 0669
 BARCLAY, M.
 0785
 BARDOS, T.J.
 0781
 BARKER, L.F.
 0723
 BARROW, R.O.
 0573
 BARRY, D.H.
 0499
 BARRY, E.J.
 0407
 BASHKAEV, I.S.
 0618
 BASOMBRIQ, M.A.
 0468
 BASSIR, O.
 0425
 BAUCHINGER, M.
 0418
 BAYRD, E.O.
 0507
 BEARD, D.
 0580, 0584
 BEARD, J.W.
 0580, 0584
 BEASLEY, J.O., III
 0737
 BEAUDREAU, G.S.
 0586
 BECK, J.S.
 0774
 BECKENBACH, H.
 0366
 BECKER, H.
 0772
 BELOHORSKY, B.
 0810

BENDER, E.
 0672
 BENDICH, A.
 0721
 BENJAMIN, T.L.
 0680, 0681
 BENNINGHOFF, O.L.
 0821
 BENTVELZEN, P.
 0627, 0629
 BERENBLUM, I.
 0420
 BERGEMANN, W.
 0765
 BERGENTZ, S.E.
 0526
 BERMAN, L.D.
 0612, 0639
 BERN, H.A.
 0769
 BERNSTEIN, I.
 0727
 BERTRAM, J.S.
 0481
 BESKROVNY, A.M.
 0457
 BETTANE, M.
 0819
 BEVILACQUA, M.
 0421
 BHASKAR, S.N.
 0737
 BIANCIFIORI, C.
 0414, 0415
 BICHEL, P.
 0824
 BIDLEMAN, K.
 0464
 BIELSCHOWSKY, M.
 0479
 BILLIAU, A.
 0685
 BIRBECK, M.S.C.
 0488
 BIRYULINA, T.I.
 0654, 0655
 BISHOP, J.M.
 0645, 0646, 0648
 BISTONI, F.
 0677
 BLACK, P.H.
 0660, 0667
 BLOEMENDAL, H.
 0607
 BLUM, E.
 0421
 BLUME, A.
 0783
 BODENBERGER, A.
 0412
 BOETTGER, D.
 0641, 0647
 BOGDEN, A.E.
 0630
 BOGOVSKY, P.A.
 0384
 BOHUON, C.
 0444
 BOIRON, M.
 0758

BOLIS, G.B.
0628, 0632
BOLONINA, N.I.
0436
BOOK, J.A.
0521
BOOTH, C.C.
0740
BOOTHE, A.O.
0563
BOREK, Z.
0768*
BORGESKOV, S.
0773
BOUCOT, K.R.
0764
BOWDEN, D.H.
0542
BRADY, R.O.
0568
BRAMBILLA, G.
0401
BRAUN, W.
0356
BRAWN, R.J.
0471
BREMNER, C.G.
0759
BRENNAN, J.T.
0524
BRESNICK, E.
0463
BRINKLEY, R.R.
0786
BRODY, I.
0735
BRODY, J.I.
0775
BROOKS, S.E.H.
0719
BROUWER, E.J.
0419
BROWER, L.P.
0512*
BROWN, E.
0364, 0365
BROWN, S.M.
0391*
BRUCKNER, L.
0768*
BRYAN, G.T.
0417, 0423
BUCCIARELLI, E.
0632
BURGER, M.M.
0679, 0680
BURGHOUTS, J.T.P.
0607
BURMEISTER, R.E.
0744
BURNET, F.M.
0355
BURNY, A.
0553
BURY, A.F.
0795
BURSTEIN, N.A.
0635
BUTEL, J.S.
0615

BUU-HOI, N.P.
0411
CALAFAT, J.
0627
CAMERON, O.A.
0548
CAMERON, E.H.D.
0782
CAMPBELL, J.A.
0620
CAMPBELL, J.L.
0825*
CANAANI, E.
0651
CARACENI, C.E.
0401
CARRUTHERS, C.
0726
CARSON, T.R.
0424
CARTER, K.L.
0488, 0610
CAULEY, T.
0486
CAVANNA, M.
0401
CEDERLOF, K.
0500
CHABOT, J.F.
0580
CHAMLIAN, D.L.
0743
CHANG, J.P.
0429
CHANG, N.H.
0551
CHANY, C.
0612
CHAPMAN, E.M.
0549
CHARUZY, I.
0449
CHERNOZEMSKI, I.N.
0399
CHERRY, C.P.
0441
CHESTERMAN, P.C.
0610
CHIRIGOS, M.A.
0602
CHOPDAR, A.
0749*
CHOPRA, H.C.
0626, 0630
CHORDI, A.
0707
CHOUROULINKOV, I.
0460
CHUAT, J.C.
0759
CHUNG, C.W.
0424
CIEGLER, A.
0388*
CISCAR RIOS, F.
0748*
CLAYSON, D.B.
0387*
CLIFFORD, P.
0574, 0578

CLIN, B.
0527*
COBB, L.M.
0543
COEZY, E.
0378*
COHEN, M.M.
0694
COHEN, S.M.
0417
CONARD, R.A.
0529
CONLEY, J.
0547
COOPER, D.A.
0764
COOPER, E.H.
0380*
CORBETT, T.H.
0400
COWAN, D.M.
0442
COYOTE, N.
0406
CRAIG, A.M.
0410
CRAIG, A.W.
0481, 0605
CRARY, D.D.
0802
CRAWFORD, J.D.
0549
CREPIN, G.
0747*
CUMAR, F.A.
0568
CUTRIGHT, D.E.
0737
DAAMS, J.H.
0627, 0629
DAGNA-BRICARELL
0699
DANNENBERG, H.
0412
DAS, K.C.
0698, 0700
DAS, M.R.
0553
DATTA, S.K.
0685
DAVEY, D.A.
0527
DAVIDSON, C.
0442
DAVIER, R.P.R.
0777
DAYAL, Y.
0426
DE BALANZO, J.
0734*
DECKER, C.
0522
DECKERS, P.J.
0728
DE COSSE, J.J.
0691
DEDUKH, N.V.
0817
DEFENDI, V.
0670

GEORGE, F.V.
 0801
 CHMANN, W.B.
 0421
 AIN, E.
 0587
 AMORE, I.W.
 0717
 GIACCO, G.S.
 0733
 AILLE, A.
 0494, 0495, 0747
 NORONHA, F.
 0711
 M.G.
 0426
 OME, K.B.
 0769
 LANC, A.
 0766
 AI, S.M.
 0652
 SCHRYVER, A.
 0579
 GRANGES, C.
 0625
 SOMER, P.
 0685
 THE, G.
 0579, 0625
 ROY, R.W.
 0388
 MOND, L.
 0346, 0445
 DWITZ, M.
 0650
 CHOWSKI, L.
 0561
 YNS, B.M.
 0529
 M.C.
 0682
 GE, W.H.
 0643
 LL, R.G.
 0590
 LEN, A.
 0700
 OV, V.K.
 0469
 INGO ALBOS, A.
 0748
 INGO GOMEZ, J.
 0748
 SCHKE, W.
 0475
 GHERTY, C.M.
 0504
 GHERTY, E., III
 0588
 Z, W.F.
 0400
 LING, M.
 0665
 ENNETTE, M.C.
 0495
 S, J.
 0696
 ESSENS, J.
 0493, 0495

DRINGS, P.
 0696
 DRUCKREY, M.
 0483
 DUBBS, D.R.
 0664, 0666
 DUBERT, J.M.
 0819
 DUESBERG, P.M.
 0651
 DUFF, R.
 0615
 DUKSIN, D.
 0661
 DULBECCO, R.
 0673, 0678
 DUNN, C.D.R.
 0413
 DUPLAN, J.F.
 0592, 0819
 DUPONT, B.
 0773
 DURR, F.E.
 0621
 DUVEL, D.
 0397
 EAST, J.
 0393
 ERBESEN, P.
 0593
 ECKER, S.
 0745
 EILBER, F.R.
 0704, 0710
 EINHORN, N.
 0578
 ELGORT, D.A.
 0596
 ELKINO, M.M.
 0524
 ELLSWORTH, H.S.
 0503
 EL'PERIN, B.M.
 0763
 ELSON, L.A.
 0413
 ENCHEV, S.
 0820
 EPLING, G.P.
 0525
 EPSTEIN, E.
 0519
 EPSTEIN, M.A.
 0619
 EPSTEIN, S.S.
 0518
 ERIKSON, E.
 0585
 ERIKSON, R.L.
 0585
 ERTURK, E.
 0417, 0423
 EVANS, A.S.
 0546
 EVANS, R.
 0725
 EWALD, J.L.
 0703
 FAHMY, M.J.
 0439

FAHMY, D.G.
 0439
 FAKHRI, O.
 0729
 FANSHIER, L.
 0645, 0646, 0648
 FARRER, J.
 0783
 FARNELL, R.L.
 0608
 FASSKE, E.
 0829
 FAVRE, M.C.
 0625
 FELDMAN, D.G.
 0550
 FERGUSON, S.W.
 0796
 FERNAGUT, A.
 0734
 FEY, F.
 0672
 FICHIDZHIAN, B.S.
 0453
 FIDLER, I.J.
 0822
 FIFL, R.J.
 0601
 FISCHER, H.
 0662
 FISHER, M.YE.
 0763
 FLODERUS, B.
 0500
 FOELSCH, E.
 0696
 FOFT, J.W.
 0396
 FOGH, H.
 0665
 FOGH, J.
 0665
 FOITZIK, E.
 0564
 FOLANOVA, K.A.
 0534
 FOOTE, F.W., JR.
 0746
 FORBES, J.F.
 0718
 FOSSATI-GUGLIELMONI, A.
 0699
 FOURCADE, A.
 0587
 FOX, R.R.
 0802
 FRABLE, W.J.
 0693
 FRADKYN, S.Z.
 0763
 FRALEY, E.E.
 0745
 FRANKE, R.
 0348
 FRANKEL, H.H.
 0409
 FRAUMENI, J.F., JR.
 0808
 FREEMAN, A.I.
 0694

FREEMAN, R.G.
0536
FREIREICH, E.J.
0798
FRIBERG, L.
0500
FRIEDMANN, T.
0684
FRIEND, C.
0603
FRIIS, R.R.
0640
FUGINAGA, K.
0584
FUJINAGA, K.
0634
FUKUDA, S.
0489
GABUNIYA, U.A.
0793
GAIDAR, E.I.
0686
GALIAN, A.
0371
GALL, S.
0787
GALLO, R.C.
0790, 0791, 0792
GARAPIN, A.C.
0648
GARIBAYAN, D.R.M.
0443
GART, J.J.
0798
GEARY, C.P.
0479
GELBOIN, H.V.
0445
GELLE, P.
0747
GENTRY, G.A.
0643
GERBER, P.
0576
GEREBTZOFF, M.A.
0469
GERWIN, B.I.
0589
GIBBS, W.N.
0719
GILBERT, E.F.
0722
GILBERT, F.
0783
GILBERT, H.S.
0359
GILDEN, R.V.
0551, 0552, 0555,
0562
GILES, A.L., JR.
0424
GIOVANELLA, B.C.
0446
GIRARDI, A.J.
0670
GLEICH, G.J.
0724
GLUCKSMANN, A.
0441
GOERTTLER, K.
0427, 0480

GOLD, P.
0358
GOLDBERG, R.I.
0754
GOLDMAN, R.L.
0622
GOODALL, C.M.
0476, 0479
GORDON, H.L.
0781
GOUTIER, R.
0544
GREEN, J.W., JR.
0403
GREEN, M.
0584, 0634
GREENBLATT, M.
0496
GREENE, E.M.
0785
GRIESEMER, R.A.
0608
GRIFFITHS, K.
0782
GRIFONI, V.
0733
GRIMMER, G.
0397
GROSS, L.
0351, 0550
GROUCHY, J.
0344
GSFELL, H.O.
0577
GUBERGRITS, M.V.
0347
GUFRIIN, M.
0460
GUPGO, C.
0634
GUTMANN, H.R.
0407
HAAG, D.
0480
HAAS, M.
0684
HAGEMAN, P.
0627
HALAWANI, A.
0771
HAMMERSTEIN, J.
0782
HANCHARD, R.
0719
HANNA, M.G., JR.
0609
HARPER, P.S.
0776
HARPER, R.M.J.
0776
HARRIS, J.W.
0503
HARRIS, R.J.C.
0642
HARTZELL, R.W.
0614
HARUNA, I.
0572
HASEGAWA, T.
0491

HASHIMOTO, N.
0394
HATANAKA, M.
0555
HAVRANKOVA, N.
0768
HAYASHI, I.
0511
HAYASHI, Y.
0491
HAYES, A.
0549
HEALEY, P.
0499
HEATH, C.M.
0456
HECKER, E.
0447, 05
HEIDELBERGER,
0400, 04
HELLMAN, K.B.
0663
HENDERSON, E.
0798
HENLE, G.
0574
HENLE, W.
0574
HERROLD, K.M.C.
0482
HESTON, W.E.
0631
HEUSON, J.C.
0450
HEYDENRICH, M.
0564
HIASA, Y.
0430
HIGGINSON, J.
0377
HIJMAN, W.
0713
HILLMAN, E.A.
0580
HIKAMATSU, T.
0511
HINONO, Y.
0539
HLOZANEK, I.
0581
HO, H.C.
0625
HOBBES, J.R.
0729
HOEFFINGER, J.
0411
HOEGLUND, S.
0613
HOERNI, B.
0354
HOFFBRAND, A.
0698, 07
HOSHINO, T.
0797
HOSHIZAKI, M.
0509
HOWEL-EVANS,
0776
HOYER, I.
0773

WINNING HEAD

F.
0812
SON, W.R.
0373
BNER, R.J.
0551, 0552, 0555,
0562, 0597
GINS, C.
0738
HES, L.E.
0454
TI, E.
0510
KKO, M.
0510
L, E.W.
0724
E, D.M.
0693
ST, L.
0433
NITSKLY, A.P.
0515
I, H.T.
0716
MURA, A.
0472
MURA, N.
0604
TITORIS, L.
0422
YA, K.
0511
NBERG, I.
0410
IKAWA, M.
0511
IMOTO, A.
0658
AELS, M.C.G.
0717
NI, S.
0797
N.
0430
Y.
0570, 0658
E, L.
0492
NKOVIC, S.
0478, 0483
MOTO, K.
0624
LON, S.
0540
KSON, J.
0645, 0646
KSON, J.F.
0807
OBS, W.H.
0722
QUIGNON, P.
0411
OFF, A.
0398
RETT, O.
0389
IU, G.
0755
EY, A., JR.
0422

JENSEN, E.M.
0626, 0630
JENSEN, K.B.
0794
JENSEN, R.
0525
JENSEN, R.D.
0808
JING, B.S.
0535
JOHANSSON, G.
0462
JOHNSON, L.I.
0391
JOHNSON, T.
0678
JONES, D.
0782
JONSSON, N.
0656
JOSEPH, W.L.
0695, 0704
KABAKOV, Y.N.
0534
KALIEV, J.
0671
KAMADA, N.
0541
KANAMARU, R.
0490
KARA, J.
0676
KARAZAS, V.
0675
KASAHARA, A.
0509
KASHA, M.
0345
KATCHALSKI, E.
0661
KATO, M.
0540
KAUFMAN, R.H.
0744
KAUFMAN, R.J.
0785
KAUFMANN, L.A.
0620
KAWASAKI, S.
0797
KAY, S.
0693
KEARNEY, R.
0454
KEITH, L.
0364, 0365
KELLOFF, G.
0551, 0552
KELLOFF, G.J.
0562
KELLY, F.
0484
KEPLINGER, M.
0421
KERCKAERT, J.P.
0495
KEHR, J.F.R.
0795
KETCHAM, A.S.
0704

KEYDAR, J.
0553
KHAN, A.U.
0345
KHUNDANOVA, L.L.
0434
KIMURA, I.
0658
KINZEL, V.
0408, 0447
KIRN, A.
0522
KIRSNER, J.B.
0528
KIRSO, U.E.
0347
KIT, S.
0664, 0666
KITAMURA, M.
0571
KITANO, Y.
0812
KLASSEN, A.
0398
KLEIN, G.
0574, 0578, 0579
KNOECHELMANN, R.
0765
KNUTSEN, T.
0576, 0798
KOBAYASHI, S.
0528
KODAMA, T.
0561
KOM, J.K.
0674
KOMONEN, A.
0530
KOLDOVSKY, P.
0669
KOLODNY, E.H.
0568
KOLOUSEK, J.
0405
KOMMINEN, V.R.C.
0496
KONISHI, Y.
0430
KOPPER, L.
0816
KOPROWSKI, H.
0669
KOROSTELEVA, T.A.
0732
KOTLER, M.
0636
KOVACS, K.
0438
KREIBICH, G.
0447, 0516
KREN, V.
0706
KRENOVA, D.
0706
KRYUKOVA, I.N.
0654
KUBIK, A.
0751
KUCEROVA, M.
0538

KUMANISHI, T.
0653
KUMKUMADZHYAN, V.A.
0453
KUROKI, T.
0490
KUROYANAGI, T.
0709
KUSTAK, R.J.
0373
KUZNETSOVA, N.N.
0655
KUZNETSOV, O.K.
0560
KWAN, H.C.
0625
KYLE, R.A.
0507
LACASSAGNE, A.
0411, 0433
LACOUR, F.
0587
LAIRD, C.W.
0802
LAMM, L.U.
0794
LANE, M.
0467
LANE, W.T.
0562
LANGE, J.
0711
LANGLOIS, A.J.
0580
LAPIS, K.
0816
LAPORTE, G.
0354
LASHER, R.
0567
LASQUELLE, F.
0758
LAWLEY, P.D.
0485
LAZAR, P.
0460
LEE, Y.K.
0551
LEENE, M.
0713
LEGATOR, M.
0484
LEGROS, N.
0450
LEHMANN, A.R.
0523
LEJNEVA, O.M.
0598
LELIEVRE, L.
0819
LEUCHTENBERGER, C.
0501
LEUCHTENBERGER, R.
0501
LEVIJ, J.S.
0449, 0451, 0452
LEVINE, W.G.
0458
LEVINSON, W.E.
0645, 0646, 0648

LEVY, J.A.
0606
LI, F.P.
0808
LIEBELT, A.G.
0467
LIEBELT, R.A.
0467
LIEGEL, J.
0446
LIJINSKY, W.
0476, 0479
LILLEHOJ, E.B.
0388
LINDAHL-KIESSLING, K.
0521, 0526
LINDEMAN, R.D.
0761
LINDHOLM, L.
0526
LINDSAY, S.
0789
LIPPINCOTT, B.B.
0404
LIPPINCOTT, J.A.
0404
LIPSCHUTZ, A.
0385
LIS, M.
0708
LODDO, S.
0766
LOER, L.A.
0703
LOMAKIN, M.S.
0455
LONBERG-HOLM, K.
0613
LUM, G.S.
0559
LYMAN, J.T.
0539
LYNN, T.N.
0796
LYSENKO, N.I.
0686
LYTLE, C.D.
0663
MAC DONALD, W.E.
0421
MAC INTOSH, I.J.C.
0527
MAC MANUS, J.P.
0818
MAC PHERSON, I.
0390
MAEDA, T.
0416
MAGEE, P.N.
0473
MAK, S.
0611
MAKAVEYEVA, M.YU.
0763
MALL, W.
0750
MALMQUIST, W.A.
0563
MALY, V.
0768

MANCONI, P.E.
0733
MANDEL, M.A.
0491
MANILDI, E.R.
0788
MANNERING, G.J.
0464
MANTOVANI, G.
0733
MARK, J.
0804, 0805
MARQUARDT, H.
0412
MARROQUIN, F.
0406
MARTYNOVA, R.P.
0826
MASHEVSKIY, A.A.
0763
MASON, M.M.
0626
MASSIMO, L.
0699
MASUDA, S.
0416
MATHIESON, B.J.
0590
MATHISEN, W.
0828
MATSUMOTO, M.
0432
MATSUYAMA, M.
0498
MATSUZAWA, A.
0633
MAUL, G.G.
0786
MAURER, L.H.
0508
MAWDESLEY-THOMAS
0499
MAZURENKO, N.P.
0595
MC DONNELL, J.P.
0648
MC DOUGALL, P.T.
0617
MC FARLAND, V.W.
0568
MC FARLANF, H.
0573
MC INTYRE, O.P.
0508
MC KINLEY, T.W.
0533
MC KISSICK, G.E.
0608
MC QUARRIE, H.G.
0503
MEDINA, A.
0821
MEIER, H.
0562, 0597
MEITES, J.
0440, 0770
MEICHERS, F.
0720

MELENDEZ, L.V.
0619
MELEWICZ, F.
0695
MELNICK, J.L.
0624
MERLIE, K.
0775
METCALF, D.
0599
METZLER, H.
0412
MEYER-BERTENRATH, J.G.
0475
MEYLER, L.
0506
MICHALK, D.V.
0427
MIDDLETON, C.A.
0714
MIDDLETON, V.L.
0714
MIDDLETON, W.R.J.
0740
MIHAILOVICH, N.
0492, 0496, 0497
MIKAT, B.
0765
MINET, P.
0469
MINOWADA, J.
0571
MINTON, J.P.
0682
MISTRY, P.B.
0592
MIYAKE, T.
0658
MIZELL, M.
0621
MIZUTANI, S.
0647
MOBBS, B.G.
0448
MODY, N.
0723
MOERTEL, C.G.
0724
MONNOT, P.
0592
MONTAGNIER, L.
0556
MONTESANO, R.
0473
MONTIEL, M.M.
0531
MONTREUIL, J.
0495
MOORE, G.E.
0571
MORA, P.T.
0568
MORGAN, D.G.
0619
MORI, M.
0784
MORIN, O.
0705
MORIYAKI, K.
0716

MORRIS, P.J.
0718
MORRIS, S.
0782
MORSE, P.A.
0807
MORSE, P.A., JR.
0643
MORTON, O.L.
0695, 0704, 0710
MOSCOVICI, C.
0583
MOTOMIYA, Y.
0511
MOUNT, B.H.
0746
MOYNE, M.A.
0819
MUELLER, R.
0577
MUNK, K.
0662
MUNSON, R.R.
0601
MUNTINGHE, O.G.
0713
MURAKAMI, N.
0823
MURANYI-KOVACS, M.I.
0378
MYERS, D.D.
0562, 0597, 0802
NAGASAWA, H.
0440, 0770
NAGATA, C.
0472
NAIMARK, A.
0542
NAKAJIMA, K.
0666
NAKAKUKI, K.
0594
NAKAYAMA, S.
0797
NAYAR, K.K.
0565
NELSON, A.I.
0519
NELSON-REES, W.A.
0591
NERUP, J.
0773
NEUMANN, H.G.
0412
NEURATH, A.R.
0614
NEWMAN, D.
0542
NGU, V.A.
0573
NIALL, H.D.
0582
NICOLLE, M.F.D.
0747
NIELSEN, M.H.
0593
NIKI, Y.
0509
NIKOLOVA, M.E.
0382

NIRENBERG, M.
0783
NIVINSKAYA, M.M.
0830
NODL, F.
0778
NOGALES FERNANDEZ, F.
0514, 0742
NOGUCHI, A.
0823
NOGUCHI, S.
0823
NOONAN, K.D.
0679
NORBERG, R.F.
0802
NORMAN, T.
0828
NORSHI, S.
0575
NORIKAT, W.
0461
NORIKH, I.R.
0454
OETJEN, L.H., JR.
0825
OKAJIMA, E.
0511
OKAZAKI, F.
0395
OLEINIK, G.I.
0686
OTA, S.
0658
ORLOV, A.B.
0732
ORMERON, M.G.
0523
OROSZLAN, S.
0552, 0567
ORR, D.J.
0485
ORTIZ DE LANDAZURI, M.
0707
OSHIMA, H.
0765
OSTERMAN, J.V.
0683
OSUNKOVA, B.O.
0573
PACHES, L.R.
0830
PALOYAN, D.
0803
PALOYAN, E.
0803
PANKOV, E.YA.
0817
PAPOYAN, S.A.
0443
PARAF, A.
0819
PARAN, M.
0779
PARODI, S.
0401
PARSONS, J.T.
0584
PARSONS, R.L.
0825

PATAN, H.M.
0722
PEARSE, A.G.E.
0740
PEGNUM, G.U.
0714
PENMAN, H.G.
0505
PERIN, F.
0411
PERIN-ROUSSEL, D.
0411
PERSSON, B.
0526
PETERS, R.L.
0562, 0602
PETROW, Z.D.
0379*
PETSKA, S.
0790
PETTERSSON, U.
0613
PFITZER, P.
0736
PHEMISTER, R.D.
0525
PHILIPSON, L.
0613
PHILLIPS, A.J.
0767*
PHILLIPS, M.W.
0788
PICKLEMAN, J.R.
0803
PIERRE, R.V.
0507
PIETERSZ, M.N.I.
0713
PILCH, Y.H.
0728
PINCUS, T.
0606
PINTADO, T.
0554
PISTER, L.
0711
PITZURRA, M.
0677
PLENERT, W.
0712
PLESCIA, O.J.
0356
PLISS, G.B.
0487
PLOEM, J.E.
0713
PLUOT, M.
0486
POEL, W.E.
0561
POLAK, J.
0799
POLLACK, R.
0558
POLLIACK, A.
0440, 0451, 0452
PONG, R.S.
0428

POPE, J.H.
0795
POPE, L.S.
0780
PORTEOUS, I.B.
0774
POUDAR, G.G.
0752
POUND, A.W.
0545
PRAGE, L.
0613
PRASAD, K.N.
0567
PREUSSMAN, R.
0478, 0483
PROLLA, J.C.
0528
PUJOL MOTX, N.
0748*
PURCHASE, I.F.H.
0402
PUVION, F.
0494, 0495
QUINTRELL, N.
0645, 0646, 0648
RABIN, M.
0650
RADOMSKI, J.
0421
RAITCHIEFF, I.
0815
RAMALINGASWAMI, V.
0426
RAPOPORT, A.M.
0808
RAPP, F.
0615
RAPP, H.J.
0727
RAPPAFORT, M.
0756
RAWLS, W.E.
0624
REDDI, A.H.
0738
REFCE, W.O.
0403
RENE, A.A.
0546
RESNITZKY, P.
0779
REVAZOVA, E.S.
0595
REY, R.K.
0634
RIRACCHI, R.
0637, 0811
RICHTER, V.R.
0497
RICKARD, C.G.
0588
RIDDICK, D.H.
0791
RIGBY, P.G.
0702
RIMAN, J.
0586
RINGERTZ, N.
0753

PIXON, R.H.
0818
ROBERTS, J.D.B.
0488
ROCA, A.N.
0535
ROIZMAN, B.
0621
ROKUTANDA, M.
0634
ROKUTANDA, M.
0634
ROMAGOSA PUIG, V.
0748*
RONDIA, D.
0459
ROSENBERG, R.
0783
ROSENGREN, B.
0526
ROSNER, F.
0363
ROSSI, G.B.
0603
ROTHSCHILD, M.
0660, 0667
ROUJEAU, J.
0371
ROUZE, P.
0819
ROWE, W.P.
0638
ROWSON, K.E.K.
0610
ROYSTON, I.
0623
ROZHKOVA, L.G.
0515*
RUBIN, A.D.
0391*
RUBIN, B.A.
0614
RUBIN, H.
0644
RUDALI, M.G.
0378*
RUDDOLPH, M.
0672
RUECKERT, F.
0508
RUECKERT, U.
0741
RWOMUSHANA, J.W.
0451
RYAN, W.L.
0702
SACHS, L.
0661, 0708
SACQUET, E.
0494
SAEGESSER, F.
0360
SAIO, S.M.
0771
SAKSELA, E.
0530
SAKURAI, M.
0800
SALAMAN, M.H.
0610

ALIER, B.
 0520*
 ANCHIS-BAYARRI LAHOZ, V.
 0730*
 ANCHIS-BAYARRI VAILLANT, V.
 0730*
 ANDER, S.
 0828*
 ANS-SABRAFEN, J.
 0748*
 ANTESSON, B.
 0521
 ANTESSON, L.
 0574
 ANTIAGO, M.
 0517*
 ARMA, P.S.
 0562, 0582
 ATO, H.
 0490
 ATPAYEVA, R.A.
 0760
 AUER, R.
 0582
 AVAGE, T.
 0621
 CANU, A.
 0803
 CHAEFER, P.K.
 0765*
 CHAEFER, W.
 0711
 CHERRER, R.
 0819
 CHLOM, J.
 0553
 CHMAEHL, D.
 0435
 CHMIDT, F.W.
 0711
 CHOLLE, R.H.
 0396
 CHRAMM, G.
 0692
 CHRAMM, T.
 0672
 CHULTE-HOLTHAUSEN, H.
 0574
 COLNICK, E.M.
 0557, 0589
 COTT, C.D.
 0503
 CRIBNER, J.
 0408
 EIFERT, E.
 0711
 ELA, B.A.
 0708
 HARON, N.
 0708
 HERBET, G.V.
 0392*
 HEVLIAGHYN, V.J.
 0675
 HEVLYAGIN, V.Y.
 0655
 HIUKASHVILLI, N.N.
 0793
 HIVELY, J.N.
 0525

SHUBIK, P.
 0513*
 SIMARD, R.
 0368
 SINGH, D.V.
 0769
 SINKS, L.F.
 0694
 SINN, I.
 0537
 SIRACKA, E.
 0810
 SIRACKY, J.
 0810
 SJOGREN, H.O.
 0656
 SKIBBA, J.L.
 0423
 SKIPSKI, V.P.
 0785
 SMIT, C.G.S.
 0506
 SMITH, C.A.
 0642
 SMITH, D.F.
 0429
 SMITH, G.H.
 0631
 SMITH, H.H.
 0539
 SMITH, J.L., JR.
 0535
 SMITH, L.H.
 0533
 SNODGRASS, M.J.
 0609
 SOHIER, R.
 0757
 SOKOLOVA, E.V.
 0455
 SOMOGYI, A.
 0438
 SOREN, L.
 0697
 SOKOKINA, Y.D.
 0477
 SPAHN, G.J.
 0602
 SPEAR, P.G.
 0621
 SPEZIA, C.A.
 0502
 SPIEGELMAN, S.
 0553
 SPJUT, H.J.
 0744
 SQUARTINI, F.
 0628, 0632
 STAEBLER, F.
 0537
 STAEMMLER, M.
 0564
 STANISLAWSKI, M.
 0819
 STANKEVICH, M.P.
 0763
 STARK, O.
 0706
 STASEK, V.
 0768*

STASINOPOULOS, M.
 0374
 STEINBERG, M.P.
 0519*
 STEPHENS, D.
 0780
 STEWART, A.M.
 0690*
 STILLMAN, A.
 0362
 STOBBE, H.
 0379*
 STOCK, C.C.
 0785
 STOKER, M.
 0350
 STOLS, A.L.H.
 0607
 STONE, N.H.
 0531
 STONE, R.A.
 0503
 STONEHILL, E.W.
 0721
 STOPCHANSKAYA, A.G.
 0686*
 STOUGHTON, R.B.
 0536
 STRAUS, F.H.
 0803
 STRUM, S.B.
 0756
 SUESS, R.
 0408, 0447
 SUGIHARA, R.
 0430
 SUGIMOTO, T.
 0431
 SUGIYAMA, H.
 0709
 SUKOVATYKH, L.S.
 0763
 SULLIVAN, D.
 0646
 SUTOW, W.W.
 0529
 SUZUKI, H.
 0498
 SUZUKI, K.
 0633
 SUZUKI, S.
 0467
 SYDOW, G.
 0739
 SYPOWICZ, D.
 0621
 SZABO, I.
 0422
 SZABO, J.
 0422
 SZENDE, R.
 0816
 TABARES, E.
 0554
 TAJIMA, H.
 0509
 TAKAYAMA, S.
 0470

TAKEBE, H.
 0489
 TAKEHARA, M.
 0657
 TAKKUNEN, J.
 0510
 TALIB, H.
 0369
 TAN, E.M.
 0536
 TANAKA, T.
 0605, 0727
 TANNOK, I.F.
 0762
 TARANCON MARTINEZ, A.
 0514*, 0742
 TARASOVA, G.V.
 0760
 TARAYAMA, H.
 0431
 TARKKANEN, J.
 0530
 TASCA, C.
 0480
 TAYLOR, A.I.
 0806
 TAYLOR, H.B.
 0743
 TELLES, N.C.
 0663
 TEMIN, H.M.
 0641, 0647
 TERADA, Y.
 0509
 TERAYAMA, H.
 0432
 TEREBUS-KEKISH, O.
 0785
 THIJS, L.G.
 0713
 THOMLEY, M.W.
 0825*
 THOMPSON, J.H.
 0502
 THORBURN, M.J.
 0719
 TING, R.C.
 0792
 TODARO, G.J.
 0557, 0589
 TOGNELLA, S.
 0733*
 TOKUNO, S.
 0666
 TOMAS, V.
 0768*
 TOMATIS, L.
 0476
 TOMINAGA, K.
 0715
 TONI, R.
 0552
 TOTH, B.
 0437, 0513*
 TOYOSHIMA, K.
 0640
 TRAHAN, E.
 0704
 TRAVNICEK, M.
 0553

TRENOELBURG, F.
 0750
 TRENTIN, J.J.
 0617
 TRKULA, D.
 0666
 TROLL, W.
 0398
 TSUCHIMOTO, T.
 0541
 TURNER, M.C.
 0562
 TURNER, W.
 0602
 TYIHAK, E.
 0816
 UCHINO, M.
 0541
 ULLYOT, J.L.
 0774
 VAGNONI, G.
 0383*
 VALLADARES, Y.
 0554
 VALYI-NAGY, T.
 0422
 VANDEPUTTE, M.
 0685
 VAN DER MAATEN, M.J.
 0563
 VAN DER WATT, J.J.
 0402
 VAN GELDER, G.
 0403
 VANGHEEL, V.
 0544
 VAN MOOSIEK, G.L., JR.
 0617
 VANHOUTE, J.J.
 0827*
 VAN KAICK, G.
 0366
 VAN NOERT, M.H.
 0567
 VARDOSANIDZE, E.S.H.
 0618
 VANGA, L.
 0700
 VAKTERESZ, V.
 0700
 VEBERT, A.
 0495
 VENABLES, C.W.
 0777
 VENKATESAN, M.
 0466, 0474
 VERGER, C.
 0587
 VERHAEGHE, M.
 0747*
 VERMEIL, C.
 0705
 VESSELINGVITCH, S.D.
 0492, 0496, 0497
 VICENTE, J.
 0381*
 VICH, Z.
 0768*
 VINCENT, M.M.
 0745

VLAEMINCK, M.N.
 0493, 0495
 VLAHAKIS, G.
 0631
 VOGEL, A.
 0558
 VOGEL, C.L.
 0723
 VOGEL, H.H., JR.
 0532
 VOGT, P.K.
 0640, 0649
 VOLFSOHN, M.I.
 0487
 VOLM, M.
 0408
 VUOPALA, U.
 0510
 WACHSMANN, F.
 0370
 WADDELL, A.
 0674, 0683
 WAGNER, E.K.
 0621
 WAHREN, B.
 0599
 WAKONIG-VAARTAU
 0809
 WALBORG, E.F.,
 0429
 WALL, A.J.
 0740
 WALLACE, M.C.
 0419
 WARWICK, G.P.
 0399
 WATANABE, I.
 0572
 WATSON, K.
 0553
 WAYSS, K.
 0408
 WERER, J.
 0611
 WEDDERBURN, N.
 0600, 0610
 WEI, L.S.
 0519*
 WEIL, R.
 0476
 WEISBURGER, E.
 0409
 WEISRUOPER, J.
 0409
 WEISS, P.A.
 0814
 WEISS, W.
 0764
 WELSCH, C.W.
 0770
 WENTON, C.E.M.
 0476
 WENZ, W.
 0366
 WEITIG, K.
 0461
 WHANG-PENG, J.
 0576, 079
 WHITFIELD, J.F.
 0818

WHITMORE, W.F.
0746
WIEBEL, F.
0445
WILBANKS, G.D.
0620
WILSON, S.
0783
WISEMAN, S.
0738
WITHERS, H.R.
0524
WOGAN, G.N.
0428
WOLMAN, S.
0558
WOOD, W.C.
0704
WOODHAM, A.A.
0387
WOODS, D.A.
0456
WOOKROOF, J.G.
0386
WRIGHT, D.H.
0689
WRIGHT, P.D.
0777
WUONG, M.D.
0433
YAMAMOTO, N.
0489

YAMAMOTO, N.S.
0409
YAMAMOTO, T.
0633, 0653
YANG, S.S.
0792
YASUZUMI, G.
0430
YOKORO, K.
0604
YOSHII, S.
0649
YOUNG, P.G.
0746
YOUNG, S.
0442
YUMOTO, T.
0561, 0569
ZADOR, S.
0465
ZAJDELA, F.
0411
ZAK, M.
0405
ZALDIVAR, M.
0532
ZAMBERNARD, J.
0567
ZAMCHECK, N.
0362

ZANETTI, M.
0583
ZAPSEPIN, N.I.
0686
ZASYPKA, A.T.
0732
ZAUN, H.
0787
ZBAR, B.
0727
ZELLJADT, I.
0626, 0630
ZEKVAS, J.D.
0717
ZEIERBERG, A.
0813
ZEVE, V.
0589
ZHUDINA, A.I.
0560
ZIANTL, F.
0712
ZIL'FYAN, V.H.
0453
ZIMMERMANN, F.K.
0412
ZIZKA, J.
0799
ZUPANOS, G.
0360
ZUR HAUSEN, H.
0574

SUBJECT INDEX

- 2-ACETYLAMINOFLUORENE
DERIVATIVES, RADIOACTIVE PRECURSOR
INCORPORATION, RNA AND DNA SYNTHESIS
(0408)
- ACTINOMYCIN
DNA SYNTHESIS, SV40 VIRUS (0662)
- ADENOCARCINOMA
COLD, URETEROSIGMOIDOSTOMY, MAN
(0825)*
EMBRYONAL, TESTS, CHILDREN (0746)
FERTILITY, ENDOMETRIAL HYPERPLASIA
(0743)
METASTASIS, THYROID, HUMAN
(0823)
PAPILLARY, GENETIC PREDISPOSITION,
FAMILIAL OVARIAN CARCINOMA (0808)
- ADENOMA
BRONCHO-ALVEOLAR CANCER, SHEEP (0820)
GASTRIC, N-METHYL-N-NITROSO-N'-
ACETYLUREA, RAT (0483)
- ADOLESCENCE
RAPID BONE GROWTH, ACUTE MYELOID
LEUKEMIA (0375)
- ADRENAL GLAND
CARCINOMA, CUSHING'S SYNDROME,
BILATERAL HYPERPLASIA, HORMONAL
THERAPY (0741)
CARCINOMA, FISSION NEUTRON IRRADIATION
(0532)
CARCINOMA, HUMAN, STEROID ANALYSIS
(0782)
ENDOCRINE LESION, URETHANE (0498)
NECROSIS, 7,12-DIMETHYLBENZ(A)ANTHRA-
CENE, RAT (0438)
- ADRIAMYCIN
BLASTOGENESIS IN HUMAN LYMPHOCYTES,
MUTAGENESIS IN HUMAN LYMPHOCYTES
(0699)
- ADSORPTION
ADENOVIRUS TYPE 7, ERYTHROCYTE (0614)
- AFLATOXIN
ASPERGILLUS FLAVUS, EFFECT OF
TEMPERATURE (0519)*
BI, ACUTE TOXICITY, KUPFFER CELL
HYPERPLASIA, BILE DUCT EPITHELIUM,
HAMSTER (0517)*
BI, B2, G1, G2, COUMARINS, FURAZOLIUM,
GUINEA PIG, HYPERSENSITIVITY (0424)
BI, ONA LIVER, RATS (0427)
BI, MICROSMAL HYDROXYLASE,
3,4-BENZOPYRENE (0428)
DIETARY, LIVER INJURY, RHESUS MONKEY
(0426)
MYCOTOXINS, TUMORIGENESIS, REVIEW
(0388)*
OILSEED PROTEINS, ANIMAL FEED,
TOXICITY, REVIEW (0387)*
PALMOTOXINS, EMBRYO LIVER (0425)
PEANUTS, DIETETICS, REVIEW (0386)*
- AGE
7,12-DIMETHYLBENZ(A)ANTHRA-
CENE, 3-METHYLCHOLANTHRENE, RAT, MOUSE
(0436)
PERINATAL PERIOD, TUMOR PROFILE,
URETHAN INDUCTION (0496)
TEEN-AGE PATIENTS, CYTOLOGIC ATYPIC,
CARCINOMA OF THE CERVIX (0744)
TUMOR SPECTRUM, URETHAN (0492)
- VARIATION, RH NEGATIVITY, LEUKEMIA
(0801)
- AGGLUTINATION
TRANSFORMED CELLS, SIMIAN VIRUS 40,
ADENOVIRUS TYPE 12, ORNITHINE,
LEUCINE POLYMER (0661)
- AIR POLLUTION
BRONCHOGENIC CARCINOMA, EPIDEMIOLOGY,
CZECHOSLOVAKIA (0768)*
CARCINOGENS, BRONCHIAL CARCINOMA,
HYDROCARBONS (0461)
LUNG CANCER, SMOKING, ITALY (0383)*
- ALDRIN
TUMORIGENICITY, DIELDRIN, ENDRIN
(0421)
- ALKYLATING AGENT
N-DIAZOACETYLGLYCINAMIDE,
N-DIAZOACETYLGLYCINE HYDRAZIDE,
CARCINOGENICITY, MOUSE (0401)
THYMUS, DNA, THERMAL DENATURATION,
CALF (0422)
- AMELOBLASTOMA
ODONTOGENIC TUMORS, ENZYME ACTIVITY
(0784)
- 4-AMINO-2',3-DIMETHYLAZOBENZENE
BINDING, LIVER PROTEIN, RAT (0432)
- AMINO ACID
ACCEPTOR RNA, AVIAN MYELOBLASTOSIS
VIRUS, AMINOACYLATION CAPACITY
(0585)
LEUKEMIC LYMPHOBLASTS, TRANSFER RNA
(0790)
- AMP
BONE MARROW, THYMUS, MITOSIS, RAT
(0818)
- ANEMIA
GASTRIC CARCINOMA, VITILIGO (0777)
- ANTIBODY
ANTISARCOMA, IMMUNITY, SKELETAL
SARCOMAS (0710)
EPSTEIN-BARR VIRUS (0757)
EPSTEIN-BARR VIRUS, CHILDREN (0758)
HEMAGGLUTINATION, INFECTIVITY, RAT
VIRUSES (0559)
HERPESVIRUS TYPE 2, INVASIVE
CERVICAL CARCINOMA (0624)
PARABLASTS, LEUKEMIA, CHILDREN,
CONTACT PERSONS (0712)
- ANTIGEN
ADENOVIRUS TYPE 12 SARCOMA, HAMSTER
(0618)
ANTI-MOUSE EGG, CYTOTOXICITY, SV40
(0669)
AUSTRALIA, PRIMARY LIVER CANCER (0724)
CARRIER AGENTS, TUMOR VACCINES (0356)
ENVELOPE-ANTIGEN RELATIONSHIPS,
HAMSTER-SPECIFIC SARCOMA VIRUSES
(0551)
GASTRIC CANCER, EMBRYONAL TISSUE,
NORMAL STOMACH, MAN (0707)
ALPHA-2-GLOBULIN, CANCER PATIENTS
URINE, IMMUNOELECTROPHORESIS (0731)
GROUP-SPECIFIC, AVIAN MYELOBLASTOSIS
VIRUS (0582)
GROUP-SPECIFIC, IMMUNOLOGICAL IDENTITY
REACTIONS, HAMSTER-SPECIFIC C-TYPE
VIRUS (0552)
GROUP-SPECIFIC, MURINE C-TYPE RNA
VIRUS (0597)
GROUP-SPECIFIC, MURINE LEUKEMIA VIRUS
(0598)

GROUP-SPECIFIC, RNA TUMOR VIRUS, VIRUS (0562)
 HEPATITIS-ASSOCIATED, HEPATOCELLULAR CARCINOMA (0723)
 HEPATOMA, DIMETHYLAMINOAZOBENZENE, DIETHYLAMINOAZOBENZENE (0434)
 HERPES SIMPLEX VIRUS, CERVICAL CARCINOMA (0623)
 HL-A, HODGKIN'S DISEASE, LEUCOCYTE PHENOTYPE (0717)
 HL-A, LEUKEMIC CELLS (0714)
 LEUCOCYTE, HODGKIN'S DISEASE (0718)
 LEUKEMIA, COMPLEMENT BINDING (0711)
 LOW-LEUKEMIC STRAIN MICE, MURINE LEUKEMIC STRAIN MICE (0596)
 3-METHYLCHOLANTHRENE, MURINE SARCOMAS (0468)
 MOUSE EMBRYO EXTRACT, CANCER TISSUE (0721)
 SHOPE PAPILLOMA VIRUS (0658)
 SPECIFICITY, CHEMICALLY-INDUCED TUMOR, VIRAL TUMORS, REVIEW (0361)
 SULFANILIC ACID-CONJUGATE, OVARIAN-ASCITES TUMOR, RAT (0732)
 TRANSPLANTATION, ADENOVIRUS SA7, HAMSTER (0616)
 TRANSPLANTATION, SV40 (0670)
 TUMOR, CELL TRANSFORMATION, SV40 (0349)
 TUMOR-SPECIFIC, ALPHA-FETOGLOBULIN, DIGESTIVE TRACT CANCER (0362)
 TUMOR-SPECIFIC ANTIGEN, ROUS SARCOMA VIRUS, MOUSE (0653)
 "VIRUS FREE" TUMORS, ROUS SARCOMA VIRUS (0655)
 AROMATIC AMINES
 GENETIC ACTIVITY, MITOTIC CONVERSION, YEAST CELLS (0412)
 AROMATIC HYDROCARBON
 INTERCALATION, POLYACENYLIC ACID (0410)
 PHOTOCARCINOGENICITY, MECHANISM (0345)
 ASCITES
 GUINEA PIG, MYCOBACTERIUM BOVIS, INHIBITION OF TUMOR GROWTH (0727)
 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE, HEPATOCARCINOMA, RAT (0429)
 ATOMIC BOMB
 SMALL G CHROMOSOME, ABERRATIONS (0541)
 AXILLA
 SARCOMA, 3,4-BENZOPYRENE, MOUSE (0467)
 AZATHIOPRINE
 CERVIX, DYSPLASIA, HUMAN (0692)
 AZO DYE
 SYNTHESIS, RAT LIVER, 4-AMINO-2',3-DIMETHYL-AZOBENZENE (0432)
 BACTERIA
 MUTANTS, 4-NITROQUINOLINE-1-OXIDE, BACTERIOPHAGE (0489)
 BENZENE HEXACHLORIDE
 ACUTE LEUKEMIA, OCCUPATIONAL EXPOSURE (0509)
 8,9-BENZO-GAMMA-CARBOLINE
 STRUCTURE-CARCINOGENICITY RELATIONSHIPS, MOUSE (0411)
 BENZO(A)PYRENE
 RNA FROM TUMOR-IMMUNE ANIMALS, TUMOR IMMUNITY TRANSFER (0728)
 WATER POLLUTION INDEX, WATER ORGANISMS, U.S.S.R. (0515)
 3,4-BENZOPYRENE
 ANTIMITOTIC EFFECT, CELL CULTURES, LUNG, RAT (0460)
 METABOLISM, CARBON MONOXIDE, LIVER, RAT (0459)
 MICROSOMAL DRUG-METABOLIZING ENZYMES, BILIARY EXCRETION (0458)
 MICROSOMAL HYDROXYLASE, AFLATOXIN B1 INHIBITION (0428)
 SARCOMA, AXILLARY REGION, MOUSE (0467)
 BLADDER
 CANCER, SEX DIFFERENCE IN INCIDENCE, CIGARETTE SMOKING (0511)
 CARCINOMA, LABORATORY WORKER, CHEMICAL CARCINOGEN (0367)
 CARCINOMA, PATHOLOGY, EPIDEMIOLOGY, REVIEW (0380)
 CARCINOMA, SCHISTOSOMIASIS (0369)
 DIBUTYLNITROSAMINE, TUMOR, MOUSE (0481)
 RAT TUMOR, RESTRICTION OF PUBLIC CONSUMPTION, CYCLAMATES (0420)
 S. HAEMATOBIIUM, CARCINOMA (0771)
 BLOOD
 CYTOMETRIC STUDY, IRRADIATED BONE MARROW LYMPHOCYTES, SPLENIC LYMPHOCYTES (0534)
 HUMAN CELL CULTURES, ULTRASOUND EXPOSURE, CHROMOSOMAL ABERRATIONS (0527)
 PERIPHERAL, BONE MARROW CELL, LEUKEMIA, HUMAN (0779)
 RH NEGATIVITY, LEUKEMIA, AGE DEPENDENT VARIATION (0801)
 BONE
 MARROW CELL, PERIPHERAL BLOOD, LEUKEMIA, HUMAN (0779)
 MARROW CELL COUNTS, X-IRRADIATION, METHIONINE SULPHOXIMINE (0405)
 MARROW TRANSPLANTATION, RADIATION INJURY, SPLENECTOMY (0533)
 OSTEOGENIC SARCOMA, EPIDEMIOLOGY, PATHOLOGY (0752)
 OSTEOSARCOMA, 32 PHOSPHORUS, ULTRA-STRUCTURE (0548)
 RAPID GROWTH, ADOLESCENCE, ACUTE MYELOID LEUKEMIA (0375)
 RNA, SARCOMA GROWTH, RAT (0817)
 TUMORS, FBV VIRUS (0561)
 XENOGENIC TRANSPLANT, OSTEOGENIC TRANSFORMATION, FIBROBLASTS (0738)
 BRAIN
 LIVER, MAMMARY TUMOR VIRUS, GR MOUSE (0629)
 5-BROMODEOXYURIDINE
 AVIAN SARCOMA VIRUS, VISIBLE LIGHT, CHICK EMBRYO FIBROBLAST (0641)
 ROUS SARCOMA VIRUS, RNA SYNTHESIS (0645)
 TRANSFORMED MOUSE KIDNEY CELLS, MITOMYCIN C, GENETIC CHANGE (0664)
 BURKITT'S LYMPHOMA
 CELL CULTURES, MITOTIC INDEX, PHYTOHEMAGGLUTININ (0730)
 EPSTEIN-BARR VIRUS, NASOPHARYNGEAL CARCINOMA, DNA (0574)
 IMMUNOSUPPRESSION, VIRUS (0687)
 LYMPHOSARCOMA, MALARIA (0689)
 MALARIAL PARASITE, COCARCINOGEN (0690)

- MEMBRANE ANTIGEN, EPSTEIN BARR VIRUS, NASOPHARYNGEAL CARCINOMA (0578)
MORPHOLOGY, EPSTEIN-BARR VIRUS (0575)
URINE AND SERUM IMMUNOGLOBULINS (0573)
VIRAL ONA DENSITY, LUCKE ADENOCARCINOMA FROG HERPESVIRUS, VIRUS, (0621)
VIRUS, EPSTEIN-BARR VIRUS, VIRAL ONA (0688)*
- CANCER
DISSEMINATED MALIGNANT DISEASES, LEUCINE AMINOPEPTIDASE ACTIVITY (0788)
ENOOMETRIUM, YOUNG WOMEN, PATHOGENESIS (0747)*
EPIDEMOLOGY, KURGAN (0754)
EPIDEMOLOGY, QUEBEC (0767)*
ETIOLOGY, HORMONAL DISORDERS, REVIEW (0385)*
MULTIPLE MALIGNANCIES, LOCALIZATION, ETIOLOGY (0772)
- CARBOHYDRATE
REPRESSION, 3-METHYLCHOLANTHRENE, OIMETHYLNITROSOAMINE DEMETHYLASE (0474)
- CARCINOGENESIS
EXPERIMENT DESIGN, CHOLESTEROL, SODIUM CYCLAMATE (0512)*
YTTERBIUM, GADOLINIUM (0403)
- CARCINOGENICITY
OIBENZACRIDINES, STRUCTURE-ACTIVITY RELATIONSHIP, SUPEROLISOLABILITY INDEX, CHEMICAL DISPLACEMENTS (0520)*
MECHANISMS, ALKYL NITROSAMINES, ELECTRONIC STRUCTURES (0472)
8-OXYQUINOLINE, MOUSE, RAT (0487)
TOBACCO CONDENSATES, ESTERASE ACTIVITY AREA TEST (0499)
- CARCINOMA
ADRENAL, HUMAN, STEROID ANALYSIS (0782)
BASAL CELL, BURN SCARS, RADIATION THERAPY (0531)
BLADDER, SCHISTOSOMIASIS (0369)
BRONCHOGENIC CARCINOMA, HISTOPATHOLOGY HUMAN (0764)
EPIDERMOID, RESPIRATORY TRACT, N-NITROSO-N-METHYLUREA, HAMSTER (0482)
ERLICH SUBCUTANEOUS, 5-N-METHYLATED LYSINE, GROWTH-PROMOTING EFFECTS (0816)
GASTRIC, GERMANY, DETECTION, MORTALITY (0765)
LIVER, RAT, N-HYDROXY-N-2-FLUORENYL-ACETAMIDE (0409)
MAMMARY GLAND, RAT, 9,10-DIMETHYL-1,2-BENZANTHRACENE (0442)
NASOPHARYNGEAL, EPSTEIN-BARR VIRUS, SURFACE ANTIGEN (0579)
NASOPHARYNGEAL CARCINOMA, BURKITT'S LYMPHOMA, EPSTEIN-BARR VIRUS, ONA (0574)
SUPERFICIAL BASAL CELL, TUMOR BUD CELL MORPHOLOGY (0735)
- CASTRATION
ESTRADIOL, THYROID, EPIDERMAL CYST, RAT (0416)
- CELL
CULTURE, 3,4-BENZANTHRACENE, ANTI-MITOTIC EFFECT, LUNG, RAT (0460)
DIFFERENTIATION, MURINE PLASMOCYTOMA, IN VITRO (0819)
FIBROBLAST, OSTEOGENIC TRANSFORMATION XENOGENIC BONE TRANSPLANTS (0738)
GROWTH, DIFFERENTIATION, HETEROTOPIA, MALIGNANCY (0379)*
POLYOMA-TRANSFORMED, GROWTH REGULATION MOUSE, HAMSTER (0350)
POPULATION KINETICS, CAPILLARY ENDOTHELIAL CELLS, MOUSE MAMMARY TUMOR (0762)
RESPONSE, ROUS SARCOMA VIRUS, SMALLPOX VACCINE VIRUS, VESICULAR STOMATITIS VIRUS (0560)
TRANSFORMATION, POLYOMA VIRUS, VIRUS GENERATION IN VITRO (0667)
TRANSFORMATION STAGES, ROUS AND POLYOMA VIRUS INDUCED, HAMSTER (0566)
TRANSFORMED, SURFACE MEMBRANE, CARBOHYDRATE (0708)
- CERVIX
CANCER, EPIDEMOLOGY, EARLY DETECTION CANADA, REVIEW (0368)
CARCINOMA, CHROMOSOME CHANGES (0809)
CARCINOMA, HERPESVIRUS ANTIGENS, HERPES SIMPLEX VIRUS (0623)
CARCINOMA, SEQUENTIAL ORAL CONTRACEPTIVE, CYTOLOGIC ABNORMALITIES (0504)
CARCINOMA, TEEN-AGE PATIENTS, CYTOLOGIC ATYPY (0744)
9,10-DIMETHYL-1,2-BENZANTHRACENE, SARCOMA, CARCINOMA, VAGINA (0441)
DYSPLASIA, AZATHIOPRINE, HUMAN (0692)
DYSPLASIA, RENAL TRANSPLANTATION, IMMUNOSUPPRESSIVE DRUGS (0693)
EPITHELIUM, HERPES SIMPLEX, HUMAN (0620)
INVASIVE CARCINOMA, HERPESVIRUS TYPE 2, ANTIBODIES (0624)
POLYPS, HYPERESTRINISM, ENDOMETRIAL HYPERPLASIA (0742)
- CHEMICAL CARCINOGENESIS
CYTOTOXIC EFFECT, CELL-CARCINOGEN INTERACTION, REVIEW (0346)
PROTEIN COMPLEXES, ACTIVITY, OVERLAP INTEGRALS (0348)
- CHEMICAL CARCINOGENS
BACTERIOPHAGE T4, MUTAGENICITY (0400)
ENVIRONMENT, COOPERATIVE RESEARCH EFFORT (0377)*
IMMUNOLOGY, REVIEW (0361)
LABORATORY WORKER, BLADDER CARCINOMA (0367)
POLYMER, SARCOMA RAT (0488)
TERATOGEN, CHEMICAL POLLUTANT (0518)*
TRANSFORMATION, REVIEW (0390)*
- CHILDREN
CHROMOSOMAL CHARACTERISTICS, NEUROGENIC TUMORS (0804)
- CHLORPROMAZINE
INHIBITION OF CARCINOGENESIS, 7,12-DIMETHYLBENZ(A)ANTHRACENE (0452)
- CHOLESTEROL
CARCINOGENESIS EXPERIMENT DESIGN, SODIUM CYCLAMATE (0512)*
DIET, LIPID, NEOPLASM, PITUITARY, LUNG

(0397)
 CHORIOCARCINOMA
 INCIDENCE IN SWEDEN, HYDATIDIFORM
 MOLE, INVASIVE MOLE (0753)
 CHROMATIN
 SEX, RADIATION, ENDOMETRIAL CANCER
 (0810)
 CHROMOSOME
 ABERRATION, HUMAN BLOOD CELL CULTURES,
 ULTRASOUND EXPOSURE (0527)
 ABERRATION, LYMPHOCYTE, CYCLAMATE
 (0418)
 ABERRATION, X-IRRADIATION IN UTERO,
 LEUCOCYTOSIS (0538)
 ABERRATIONS, ADENOVIRUS, VIRUS (0686)*
 ABERRATIONS, COBALT 60 IRRADIATION,
 3H-URICINE IRRADIATION (0521)
 ABERRATIONS, SMALL G, ATOMIC BOMB
 SURVIVORS (0541)
 ABERRATIONS, SV40, MYCOPLASMA (0665)
 ABNORMALITIES, ORAL CONTRACEPTIVES
 (0503)
 ABNORMALITY, MYELOMA, HUMAN (0797)
 ALTERATION IN NUMBER, MYELOMA, MSCP-1
 TUMOR, MOUSE (0716)
 ALTERATIONS, CERVICAL CARCINOMA (0809)
 C-GROUP, LEUKEMIC REACTION, MYELOPRO-
 LIFERATIVE DISEASE (0799)
 C MARKER, EPSTEIN-BARR VIRUS (0576)
 DR-- AND DR--, RETINOBLASTOMA,
 DEVELOPMENTAL ABNORMALITIES (0806)
 HEMATOLOGICAL DISORDERS, PRELEUKEMIA
 (0800)
 KARYOTYPE, NEUROGENIC TUMORS, CHILDREN
 (0804)
 KARYOTYPE, TUMOR TRANSPLANTABILITY,
 FERRIOEXTRAN SPOFA-INDUCED SARCOMA
 (0706)
 KARYOTYPE ANALYSIS, ABERRATIONS,
 SPORADIC RETINOBLASTOMA (0805)
 KARYOTYPES OF TUMOR CELLS, ROUS
 SARCOMA VIRUS (0591)
 N-METHYL-N'-NITRO-N-NITROSOGUANIDINE,
 CELL CYCLE, EMBRYONIC LUNG CELL
 (0484)
 MODALITY, HEPATOMA, CYSTEINE
 DESULFURASE, BETA-MERCAPTOPYRUVATE
 DESULFURASE, RAT (0807)
 MODALITY, REVERSION, SV40 VIRUS,
 POLYOMA VIRUS, MOUSE CELL LINE
 (0558)
 MUTATION, DIMETHYLBENZANTHRACENES,
 DROSOPHILA MELANOGASTER (0439)
 PHILADELPHIA, CHRONIC MYELOID LEUKEMIA
 CYTOGENETICS, CARCINOGENESIS (0344)
 PHI, ANEUPLOIDY, ACUTE MYELOGENOUS
 LEUKEMIA (0798)
 COCARCINOGEN
 MALARIAL PARASITE, BURKITT'S LYMPHOMA
 (0690)*
 PHORBOL MYRISTATE ACETATE, PROMOTER
 (0398)
 COLON
 CARCINOMA, URETEROSIGMOIDOSTOMY,
 MAN (0825)*
 FAMILIAL POLYPOSIS, TERMINAL ILEUM,
 POLYPOID LYMPHOID HYPERPLASIA
 (0827)*
 CONCAVALIN A
 AGGLUTININ, CONTACT INHIBITION,

POLYOMA VIRUS (0679)
 CONJUNCTIVA
 MALIGNANT MELANOMA (0749)*
 COUMARIN
 AFLATOXINS, FURAZOLIUM, GUINEA PIG,
 HYPERSENSITIVITY (0424)
 CROTON OIL
 PHORBOL DERIVATIVES, TRITIUM LABELING
 TECHNIQUE (0516)*
 SKIN TUMOR, UV IRRADIATION, ACETIC
 ACID, XYLENE (0545)
 CYCLAMATE
 HEPATOMAS, PULMONARY TUMORS, MOUSE,
 REVIEW (0378)*
 LYMPHOCYTES, CHROMOSOME ABERRATIONS
 (0418)
 METABOLISM IN RAT, DIET (0419)
 RAT BLADDER TUMORS, RESTRICTION OF
 PUBLIC CONSUMPTION (0420)
 CYCLOPHOSPHAMIDE
 METASTASIZING OVARIAN CARCINOMA, ACUTE
 MYELOGENOUS LEUKEMIA (0506)
 CYTOTOXICITY
 SV40, ANTI-MOUSE EGG ANTIGEN (0669)
 DDT
 CHLOROPHENOTHANE, ACUTE LEUKEMIA,
 OCCUPATIONAL EXPOSURE (0509)
 DEPIGMENTATION
 EFFECT, 9,10-DIMETHYL-1,2-BENZANTHRA-
 CENE, EPIPHYSECTOMY, BENZANTHRACENE,
 HAMSTER (0444)
 DERMATOGLYPHIC PATTERNS
 LEUKEMIA, GENETIC FACTOR (0363)
 DIRENZACRIDINE
 CARCINOGENIC POTENCY, STRUCTURE
 ACTIVITY RELATIONSHIPS, CHEMICAL
 DISPLACEMENTS, SUPERISOLCABILITY
 INDEX (0520)*
 DIETHYLNITROSAMINE
 BLADDER, TUMOR, MOUSE (0481)
 DIET
 CYCLAMATE, METABOLISM IN RAT (0419)
 DIETHYLNITROSAMINE
 PAPILLOMATA, TRACHEAL MUCOSA, CYTO-
 PHOTOMETRY, GLODEN HAMSTER (0480)
 RIBOSOMAL FERRITIN, RAT LIVER (0475)
 DIFFERENTIATION
 CELL COLONY-FORMING ABILITY, FRIEND
 LEUKEMIA VIRUS (0603)
 MAMMARY GLAND, LOBULOALVEOLAR, MOUSE
 STRAIN DIFFERENCES, HORMONE (0769)
 TRACHEAL MUCOSA, DIETHYLNITROSAMINE,
 GLODEN HAMSTER, TRACHEAL MUCOSA
 (0480)
 TROPHOBLASTIC, GONADOTROPHIN SECRETION
 BRONCHIAL CARCINOMA (0774)
 DIGESTIVE TRACT
 TUMOR SPECIFIC ANTIGENS, ALPHA-
 FETOGLOBULIN (0362)
 DIGIT FIBROUS TUMOR
 CYTOPLASMIC INCLUSIONS, VIROLOGICAL
 STUDY (0795)
 DIMETHYLAMINOAZOBENZENE
 CARCINOGENESIS INHIBITION, NAPHTHYLISO-
 THIOCYANATE, LIVER, RAT (0433)
 DIETHYLAMINOAZOBENZENE, HEPATOMA,
 ANTIGENS (0434)
 4-DIMETHYLAMINOSTILBENE
 SKIN TUMORS, RAT (0470)
 DIMETHYLBENZ(A)ANTHRACENE

LYMPHATIC URIDINE UPTAKE, ANTI-LYMPHOCYTE SERUM (0456)
 MAMMARY GLAND, CARCINOMA, RAT, INSULIN (0450)
 TESTOSTERONE, MAMMARY ADENOCARCINOMA (0448)
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 ADRENALS, NECROSIS, STEROID, RAT (0438)
 7-BROMO-METHYL-12-METHYLBENZANTHRACENE
 1,7-DIMETHYLBENZANTHRACENE,
 3,9-DIMETHYLBENZANTHRACENE,
 CHROMOSOME, MUTATION, DROSOPHILA
 MELANOGASTER (0439)
 CANCER, LIP MUCOSA, HAMSTER (0453)
 CARCINOGENESIS, AGE DEPENDENCE, MOUSE,
 RAT (0436)
 CARCINOGENICITY, GUINEA PIGS (0437)
 CARCINOMA, MAMMARY GLAND, RAT (0442)
 CASTRATED AND INTACT HAMSTERS, TESTOSTERONE (0449)
 CERVIX, VAGINA (0441)
 CHLORPROMAZINE, INHIBITION OF CARCINOGENESIS (0452)
 CORTISONE ACETATE, INHIBITION OF CARCINOGENESIS (0451)
 EPIPHYSECTOMY, BENZANTHRACENE,
 DEPIGMENTATION EFFECT, HAMSTER (0444)
 MAMMARY GLAND, CARCINOMA, IMMUNOLOGY,
 RAT (0454)
 MAMMARY GLAND, HORMONAL ANTITUMOR
 THERAPY, RAT (0457)
 SARCOMA, IMMUNIZATION, RAT (0455)
 SKIN, ARYL HYDROCARBON HYDROXYLASE,
 7,8-BENZOFLAVONE, MOUSE (0445)
 SKIN SUSCEPTIBILITY, HAIR FOLLICLE
 CYCLE, MOUSE (0443)
 SKIN TUMOR, POLYINOSINIC ACID/
 POLYCYTIDYLIC ACID, RNA, PHORBOL
 ESTER, MOUSE (0447)
 SUSCEPTIBILITY TO TUMOR INDUCTION,
 HAIRLESS MICE (0444)
 DIMETHYLNITROSAMINE
 METABOLISM, NUCLEIC ACID METHYLATION
 (0473)
 RIOPELLE'S TUMOR, HISTOGENESIS,
 REVIEW (0371)
 TRANSPLACENTAL EFFECT, EPITHELIAL
 HYPERPLASIA, PAPILLARY NEOPLASIA,
 KIDNEY, MOUSE (0477)
 4(5)-(3,3-DIMETHYL-1-TRIAZENO)IMIDAZOLE-
 5(4)-CARBOXAMIDE
 MAMMARY ADENOCARCINOMA, THYROID
 LYMPHOSARCOMA (0423)
 DISEASE
 HEMATOLOGICAL DISORDER, CHROMOSOME
 ABNORMALITY, HUMAN, LEUKEMIA (0800)
 SCHISTOSOMIASIS, BLADDER, CARCINOMA
 (0369)
 DNA
 ALVEOLAR CELL CARCINOMA, ALVEOLAR
 MACROPHAGE (0736)
 DOUBLE-STRAND BREAKS, X-IRRADIATION,
 MURINE LYMPHOMA CELLS (0523)
 E. COLI, N-METHYL-N'-NITRO-N-NITROSO-
 GUANIDINE, METHYLATION (0485)
 EPSTEIN-BARR VIRUS, VIRUS, BURKITT'S
 LYMPHOMA (0688)*

INTERFERON, POLYOMA VIRUS, TEMPERATURE
 SENSITIVE POLYOMA MUTANT, 3T3 CELL
 CULTURE (0678)
 METABOLISM, AFLATOXIN B1, METHYL-
 AZOXYMETHANOL-ACETATE, ETHYLNITRO-
 SOUREA (0427)
 NUCLEAR, UV RADIATION, PHOTOCHEMICAL
 LESION, MOUSE (0536)
 PAPILLARY THYROID CARCINOMA, HUMAN
 (0789)
 POLYMERASE, AVIAN MYELOBLASTOSIS
 VIRUS, RNA (0584)
 POLYMERASE, LYMPHOCYTE TRANSFORMATION,
 PHYTOHEMAGGLUTININ STIMULATION,
 REPLICATION (0703)
 POLYMERASE, MURINE SARCOMA VIRUS,
 VIRUS, RNA (0634)
 POLYMERASE ACTIVITY, C-TYPE RNA VIRUS
 (0555)
 REPLICATION, FROG VIRUS 3, VIRUS,
 GAMMA RAYS (0522)
 SYNTHESIS, ACETAMIDOFUORENE DERIVATIVES
 (0408)
 SYNTHESIS, ACTINOMYCIN D, SV40 VIRUS
 (0662)
 SYNTHESIS, CELL DENSITY, EPITHELIUM
 (0813)
 SYNTHESIS, CHICK EMBRYO CELL CULTURE
 ROUS SARCOMA VIRUS, AVIAN LEUKOSIS
 VIRUS (0566)
 SYNTHESIS, GLUCOSE METABOLISM,
 LEUKEMIA AND DIABETES (0775)
 SYNTHESIS, LYMPHOCYTE TRANSFORMATION,
 ALPHA-AMINO-P-TOLVENESULFONAMIDE,
 HUMAN (0508)
 SYNTHESIS, MEGALOBlastic ANEMIA,
 PHYTOHEMAGGLUTININ-TRANSFORMED
 LYMPHOCYTE (0698)
 SYNTHESIS, MOUSE KIDNEY CELL CULTURE
 POLYOMA VIRUS, T-ANTIGEN (0676)
 SYNTHESIS, PHYTOHEMAGGLUTININ,
 LYMPHOCYTES, EXTRACORPOREAL IRRADIATION
 OF BLOOD (0526)
 THERAPY, POLYOMA PSEUDOVIRUS, UNCOA
 IND, DNASE (0683)
 THERMAL DENATURATION, THYMUS, CALF,
 ALKYLATING AGENTS (0422)
 TRANSFORMATION SUSCEPTIBILITY, SV40
 (0659)
 VIRAL, DENSITIES, LUCKE ADENOCARCINOM,
 FROG HERPESVIRUS, BURKITT'S LYMPHOMA
 (0621)
 DYSPLASIA
 CERVIX, AZATHIOPRINE, HUMAN (0692)
 ECOLOGY
 CARCINOGENIC FACTORS, REVIEW (0384)
 CARCINOGENIC HYDROCARBONS, WATER
 POLLUTION INDEX, BENZO(A)PYRENE,
 U.S.S.R. (0515)*
 EMBRYO
 ANTIGEN, GASTRIC CANCER, MAN (0707)
 ENDOCRINE GLAND
 PINEAL GLAND, 9,10-DIMETHYL-1,2-
 BENZANTHRACENE, DEPIGMENTATION
 RESPONSE, HAMSTER (0444)
 ENDOMETRIUM
 CANCER, SEX CHROMATIN, RADIATION
 (0810)
 CANCER, YOUNG WOMEN, PATHOGENESIS
 (0747)*

HYPERPLASIA, ADENOCARCINOMA, FERTILITY (0743)
 VIRUS, HERPESVIRUS (0622)
 ENVIRONMENT
 COOPERATIVE RESEARCH EFFORT, CHEMICAL CARCINOGENS (0377)*
 ISOLYME
 ACETYLCHOLINESTERASE, NEUROBLASTOMA, MOUSE (0783)
 ALKALINE PHOSPHATASE, SUCCINIC DEHYDROGENASE, N-NITROSO-N-METHYL-URETHANE, LUNG HISTOLOGY, MOUSE (0486)
 ALKALINE PHOSPHATASE, THYMIC LYMPHOMA, MURINE LEUKEMIA VIRUS, RAT (0590)
 ARYL HYDROCARBON HYDROXYLASE, SKIN, MOUSE, 9,10-DIMETHYLBENZANTHRACENE, 7,8-BENZOFLAVONE (0445)
 BENZOPYRENE HYDROXYLASE, CARBON MONOXIDE, LIVER, RAT (0459)
 CYSTEINE DESULFURASE, BETA-MERCAPTO-PYRUVATE DESULFURASE, CHROMOSOME MODALITY, HEPATOMA, RAT (0807)
 DIMETHYLNITROSAMINE DEMETHYLASE, 3-METHYLCHOLANTHRENE, CARBOXYRATE REPRESSION (0474)
 DIMETHYLNITROSAMINE DEMETHYLASE, RAT LIVER, 3-METHYLCHOLANTHRENE (0466)
 DNA POLYMERASE, ROUS SARCOMA VIRUS (0648)
 ENDONUCLEASE, KIDNEY CELL CULTURE, HAMSTER, POLYOMA VIRUS (0674)
 ENZYMATIC BLOCK, GANGLIOSIDE SYNTHESIS, DNA VIRUS-TRANSFORMED CELL LINES (0568)
 GLUTAMATE, SUCCINATE, LACTATE, ISOCITRATE GLUCOSE-6-PHOSPHATE DEHYDROGENASES, SKIN, METHYLCHOLANTHRENE, MOUSE (0469)
 GLYCOLYTIC, HEPATOMA, RAT, TUMOR GROWTH (0739)
 LEUCINE AMINOPEPTIDASE ACTIVITY, DISSEMINATED MALIGNANT DISEASES (0788)
 MICROSOMAL DRUG-METABOLIZING ENZYMES, BILIARY EXCRETION, 3,4-BENZOPYRENE (0458)
 MICROSOMAL HYDROXYLASE, 3,4-BENZOPYRENE, AFLATOXIN B1 (0428)
 ONTOGENIC AMELOBLASTIC TUMORS, HISTOCHEMISTRY (0784)
 PHOSPHOGLUCOMUTASE ISOZYME, CHRONIC LYMPHATIC LEUKEMIA (0794)
 POLYMERASE, ENDONUCLEASE, RNA, DNA, ROUS SARCOMA VIRUS (0647)
 POLYMERASE, NUCLEIC ACID, ONCOGENIC VIRUS (0553)
 POLYMERASE, RNA, DNA, AVIAN MYELOBLASTOSIS (0586)
 POLYMERASE, RNA, DNA, ROUS SARCOMA VIRUS (0651)
 REVERSE TRANSCRIPTASE, HUMAN LEUKEMIA VIRUSES, VIRUS (0352)
 RIBONUCLEOTIDE REDUCTASE, CELL EXTRACT, NEOPLASTIC TISSUE, HUMAN (0781)
 RNA-DEPENDENT, DNA POLYMERASE, RNA VIRUS, ONCOGENIC VIRUS (0557)
 THYMIDINE KINASE, KIDNEY CELL, SV40 VIRUS, HAMSTER (0667)

TRANSFER RNA METHYLASE ACTIVITY, GROWTH AND DIFFERENTIATION, NORMAL AND NEOPLASTIC TISSUE SYSTEMS (0791)
 TYROSINE HYDROXYLASE, CELL-FREE EXTRACT, NEUROBLASTOMA (0567)
 EPIDEMOLOGY
 BRONCHOGENIC CARCINOMA, AIR POLLUTION, CZECHOSLOVAKIA (0768)*
 CANCER, CHILD, CANADA (0755)
 CANCER, KURGAN (0754)
 CANCER, QUEBEC (0767)*
 CARCINOGENIC FACTORS, ECOLOGY, REVIEW (0384)*
 CERVICAL CANCER, CANADA, PRECLINICAL STAGE DETECTION, REVIEW (0368)
 CHILDHOOD CANCER INCIDENCE, CANCER MORTALITY, ATOMIC BOMB IRRADIATION (0540)
 DEATH RATES, HEMATOPOIETIC CANCER, OKLAHOMA (0761)
 ESOPHAGEAL CANCER, KAZAKHSTAN (0760)
 GASTRIC CARCINOMA, GERMANY, DETECTION, MORTALITY (0765)*
 PATHOLOGY, BLADDER CARCINOMA, REVIEW (0380)*
 PATHOLOGY, OSTEOGENIC SARCOMA (0752)
 PULMONARY CANCER INCIDENCE, SARONIA, TUMOR MORBIDITY DATA (0766)*
 SWEDEN, CHORIOCARCINOMA, HYDATIDIFORM MOLE (0753)
 EPIDERMIS
 UREA-EXTRACTABLE ANTIGENS, BENIGN AND MALIGNANT TUMORS, MOUSE (0726)
 EPIGENESIS
 NEOPLASTIC TRANSFORMATION, EMBRYONIC SYSTEMS, REVIEW (0392)*
 EPITHELIUM
 MOUSE KIDNEY, CELL DENSITY, PROLIFERATION (0813)
 OROPHARYNGEAL TUMOR, FACIAL TUMOR, MOUSE, N-NITROSOPENTAMETHYLENEIMINE, N-NITROSOHEXAMETHYLENEIMINE (0479)
 ERYTHROCYTE
 ADENOVIRUS TYPE 7, VIRAL ADSORPTION (0614)
 ESOPHAGUS
 CANCER, FAMILIAL INCIDENCE, EPIDEMOLOGY, KAZAKHSTAN (0760)
 CARCINOMA, TYLOSIS, GENETIC LINKAGE (0776)
 ESTRADIOL
 CASTRATION, THYROID, EPIDERMOID CYST, RAT (0416)
 DL-ETHIONINE
 HYPERPLASTIC NODULE, RAT LIVER (0430)
 ETHYL-NITROSOUREA
 CANCER, TRANSPLACENTAL CARCINOMA, RATS (0478)
 DNA, LIVER (0427)
 EYE
 CARCINOMA IN CATTLE, HIGH-VOLUME FEEDING (0780)
 FACE
 LIP, RADIATION THERAPY, MELANOMA (0547)
 FEMUR METAPHYSIS
 BETA-RADIATION, EXPERIMENTAL OSTEOSARCOMA, RAT (0543)
 FERRIDEXTRAN SPOFA
 SARCOMA, TUMOR TRANSPLANTABILITY,

KARYOTYPE (0706)
 FERRITIN
 RIBOSOMAL, RAT LIVER, CARCINOGENS (0475)
 FERTILITY
 ENDOMETRIAL HYPERPLASIA, ADENOCARCINOMA (0743)
 FIBROBLAST
 EMBRYONIC HUMAN FIBROBLAST, POLYOMA VIRUS, ROUS SARCOMA VIRUS, SENDAI VIRUS (0675)
 FIBROMA
 ESTROGENS, POLYETHYLENE STRIPS, UTERINE TUBES, GUINEA PIG (0815)
 2-FLUORENYLACETAMIDE
 HYPERPLASTIC NODULE, RAT LIVER (0430)
 FOLIC ACID
 UPTAKE, PHYTOHEMAGGLUTININ, HUMAN LYMPHOCYTES (0701)
 FREUND ADJUVANT
 PLASMA CELL TUMOR, MICE (0395)
 PLASMACYTOMA, MICE (0394)
 FURAZOLIAM
 COUMARINS, AFLATOXINS, GUINEA PIG, HYPERSENSITIVITY (0424)
 GADOLINIUM
 CARCINOGENESIS, YTTERBIUM (0403)
 GANGLIOSIDE
 SYNTHESIS, DNA VIRUS-TRANSFORMED CELL LINES, ENZYMATIC BLOCK (0568)
 GASTROINTESTINAL TRACT
 PAPILLOMA, CARCINOMA, NITROSAMINE (0476)
 TRANSPLACENTAL INDUCTION, RATS, ETHYL NITROSOUREA (0478)
 GENETICS
 CARCINOMA OF THE ESOPHAGUS, TYLOSIS (0774)
 CYTOGENIC ABNORMALITY, AFFECTED SIBLINGS, LYMPHOSARCOMA (0694)
 ESOPHAGUS, FAMILIAL INCIDENCE, EPIDEMIOLOGY, KAZAKHSTAN (0760)
 FAMILIAL AGGREGATION, ACUTE LYMPHO-CYTIC LEUKEMIA (0796)
 FAMILIAL POLYPOSIS, POLYPOID LYMPHOID HYPERPLASIA, TERMINAL ILEUM (0827)*
 FAMILIAL VON HIPPEL-LINDAU'S DISEASE, PHEOCHROMOCYTOMA (0828)*
 LEUKEMIA, DERMATOGLYPHIC PATTERNS (0363)
 LYMPHOSARCOMA, RABBIT (0802)
 MITOTIC CONVERSIONS, YEAST CELLS, AROMATIC AMINES (0412)
 PREDISPOSITION, PAPILLARY ADENOCARCINOMA, FAMILIAL OVARIAN CARCINOMA (0808)
 STRAIN DIFFERENCES, IMMUNOPATHOLOGICAL PROFILE, TUMOR PROFILE, REVIEW (0393)*
 SUSCEPTIBILITY, THYMIC LYMPHOMA, CELL-FREE THYMIC SUPERNATANT (0594)
 SUSCEPTIBILITY TRANSMISSION, MAMMARY TUMOR VIRUS, MILK TRANSMISSION (0631)
 TRANSMISSION, MOUSE MAMMARY TUMOR VIRUS (0627)
 TWIN, CANCER INCIDENCE (0365)
 TWIN, LEUKEMIA, REVIEW (0364)
 TWIN METHOD, CANCER INCIDENCE, SMOKING (0500)

TWIN ZYGOSITY, CONCORDANCE DETERMINATION, NEOPLASTIC DISEASE (0826)*
 GLYCINE DERIVATIVES
 N-DIAZOACETYLGLYCINAMIDE, N-DIAZOACETYLGLYCINE HYDRAZIDE, CARCINOGENICITY, MOUSE (0401)
 GLYCOLYSIS
 HEPATOMA, RAT, TUMOR GROWTH (0739)
 GRANULOMA
 PLASMA CELL, MINERAL OIL TUMOR INDUCTION, VIRUS-LIKE PARTICLES (0396)
 GROWTH
 DIFFERENTIATION, NORMAL AND NEOPLASTIC TISSUE, TRANSFER RNA METHYLASE ACTIVITY (0791)
 DYNAMICS, WALKER'S CARCINOMA, GASTRIC WALL, RAT (0763)
 INHIBITION, AGGLUTININ, POLYOMA VIRUS, CONCANAVALIN A (0679)
 MALIGNANCY, DIFFERENTIATION, HETEROTOPIA (0379)*
 OVERGROWTH STIMULATING ACTIVITY, ROUS SARCOMA VIRUS, SONIC DISRUPTION OF CELLS (0644)
 POLYOMA VIRUS, 3T3 AND BALB LINES, MITOSIS, MORPHOLOGY (0673)
 PROMOTING EFFECTS, ERLICH SUBCUTANEOUS CARCINOMA, 5-N-METHYLATED LYSINE (0816)
 REGULATION, POLYOMA-TRANSFORMED, MOUSE, HAMSTER (0350)
 HAIR
 7,12-DIMETHYLBENZ(A)ANTHRACENE, SUSCEPTIBILITY TO TUMOR INDUCTION, HAIRLESS MICE (0446)
 FOLLICLE CYCLE, SKIN SUSCEPTIBILITY, 7,12-DIMETHYLBENZ(A)ANTHRACENE, MOUSE (0443)
 HEMATOPOIESIS
 PHYTOHEMAGGLUTININ-STIMULATED LYMPHOCYTES, HEME-SYNTHESIS (0700)
 HEPATOMA
 CYSTEINE DESULFURASE, BETA-MERCAPTOPYRUVATE DESULFURASE, CHROMOSOME MODALITY, RAT (0807)
 GLYCOLYTIC ENZYMES, RAT, GROWTH (0739)
 PREDNISOLONE, RNA SYNTHESIS, DNA SYNTHESIS, PHYTOHEMAGGLUTININ (0696)
 PULMONARY TUMORS, CYCLAMATE, MOUSE, REVIEW (0378)*
 HETEROKARYOCTE
 ADENOVIRUS 12, PERMISSIVE AND NON-PERMISSIVE CELL FUSION (0611)
 HEXOSE
 PROTEIN-BOUND NEUTRAL, RADIATION, HEPATOCYTIC ULTRASTRUCTURAL CHANGES (0546)
 HISTOGENESIS
 EMBRYONAL ADENOCARCINOMA, TESTIS, CHILDREN (0746)
 HISTOPATHOLOGY
 HODGKIN'S DISEASE, PATHOGENESIS, MAN (0744)*
 HODGKIN'S DISEASE
 CHILDREN, INCIDENCE AND PATHOLOGY (0754)
 HISTOPATHOLOGY, PATHOGENESIS, MAN (0744)*
 HL-A ANTIGEN SPECIFICITY (0717)

EUCOCYTE ANTIGENS (0718)
 LYMPHOCYTES, PHYTOHEMAGGLUTININ CON-
 SUMPTION (0733)
 LYMPHOSARCOMA, WALDENSTROM'S MACRO-
 GLOBULINEMIA, PLASMOCYTOMA,
 RETICULOSARCOMA, IMMUNOGLOBULINS
 (0734)
 LYMPH INVOLVEMENT, SPREAD, MECHANISM
 (0821)
 HORMONE
 ANTITUMOR EFFECT, 7,12-DIMETHYLBENZ-
 (A)ANTHRACENE, MAMMARY GLAND, RAT
 (0457)
 CANCER ETIOLOGY, MAN, REVIEW (0385)*
 CHANGES, CANCER PATIENTS, DISCRIMINANT
 FUNCTION (0372)
 CONTRACEPTIVES, CERVIX, UTERUS,
 EPITHELIAL ATYPIAS, HUMAN (0514)*
 ESTROGENS, POLYETHYLENE STRIPS,
 UTERINE TUBES, GUINEA PIG (0815)
 GONADOTROPHIN SECRETION, TROPHOBLASTIC
 DIFFERENTIATION, BRONCHIAL CARCINOMA
 (0774)
 HYPERESTRINISM, PROGESTATIONAL
 DEFICIENCY, ENDOMETRIAL HYPERPLASIA,
 CERVICAL POLYPS (0742)
 HYPOTHALAMIC LESION, PROLACTIN, RAT
 MAMMARY TUMOR (0770)
 LOBULOALVEOLAR DIFFERENTIATION, MOUSE
 STRAIN DIFFERENCES (0769)
 PLASMA GROWTH, HYPERTROPHIC OSTEO-
 ARTHROPATHY, CARCINOMA OF THE
 BRONCHUS (0773)
 PROLACTIN, MAMMARY CARCINOGENESIS
 INHIBITION (0440)
 RAT LIVER, POLYRIBOSOMES, X-IRRADIATION
 (0544)
 DIAZINE SULFATE
 LUNG, LIVER, CARCINOMA, MOUSE,
 ISONIAZIDE METABOLISM, MAN (0415)
 LUNG CANCER, GONADECTOMY, MOUSE (0414)
 CARBON
 POLYCYCLIC, CARCINOGENS, BRONCHIAL
 CARCINOMA (0461)
 POLYCYCLIC, PLANTS, AIR POLLUTANTS,
 FOOD (0397)
 2-HYDROXY-ACETYLAMINOFLUORENE
 BINDING TO POLYRIBONUCLEOTIDES IN
 VITRO (0406)
 2-HYDROXY-N-2-FLUORENYLACETAMIDE
 CARCINOMA, LIVER, RAT (0409)
 PROTEIN ADDUCT, LIVER, RAT (0407)
 HYPERPLASIA
 ENDOMETRIAL, HYPERESTRINISM, CERVICAL
 POLYPS (0742)
 INFLAMMATORY PAPILLARY, ORAL MUCOSA,
 DENTURE IRRITATION (0737)
 KUPFFER CELL, BILE DUCT EPITHELIUM,
 AFLATOXIN B1, HAMSTER (0517)*
 CARCINOGENIC CANCER
 MULTIPLE MYELOMA, ACUTE MYELOMONOCYTIC
 LEUKEMIA, MELPHALAN (0507)
 THYROTOXICOSIS, RADIOACTIVE IODINE
 TREATMENT (0549)
 IMMUNITY
 ADENOVIRUS SA7, HAMSTER (0616)
 ANTISARCOMA ANTIBODY, SKELETAL SARCOMA
 (0710)
 MOLONEY VIRUS, RAUSCHER VIRUS, MOUSE
 (0635)
 SARCOMA TRANSPLANTATION, YEAST, MOUSE

(0705)
 SULFANILIC ACID-CONJUGATED ANTIGENS,
 OVARIAN ASCITES TUMOR, RAT (0732)
 TRANSFER, RNA FROM TUMOR-IMMUNE
 ANIMALS, BENZ(A)PYRENE (0728)
 IMMUNOGLOBULIN
 BIOSYNTHESIS, PLASMA CELL, MYELOMA
 (0720)
 LYMPHOSARCOMA, WALDENSTROM'S
 MACROGLOBULINEMIA, PLASMOCYTOMA,
 HODGKIN'S DISEASE (0734)
 URINE AND SERA, BURKITT'S LYMPHOMA
 (0573)
 IMMUNOLOGY
 ANTITHYMOCYTE SERUM, SPLENIC LYMPHOID
 TUMORS, POLYOMA VIRUS (0682)
 CARRIER AGENTS, TUMOR VACCINES, ANTI-
 GENIC "OTHERNESS" (0356)
 CHEMICALLY-INDUCED TUMORS, VIRAL
 TUMORS, REVIEW (0361)
 CROSS IMMUNIZATION, VIRUS, MURINE
 LEUKEMIA VIRUS, INTERFEROGENESIS
 (0595)
 7,12-DIMETHYLBENZ(A)ANTHRACENE,
 GAMMA-2-GLOBULIN, FREUND ADJUVANT,
 METASTASES, RAT (0455)
 EMBRYO SPECIFIC ANTIGEN, CANCER TISSUE
 MOUSE (0721)
 FERRIOEXTRAN SPOFA-INDUCED SARCOMA,
 TRANSPLANTABILITY, KARYOTYPE (0706)
 GAMMA-2-GLOBULIN, URINE, IMMUNO-
 ELECTROPHORESIS (0731)
 HAMSTER-SPECIFIC C-TYPE VIRUS, GROUP
 SPECIFIC VIRION ANTIGEN (0552)
 IMMUNE DEFICIENCIES, TUMORIGENESIS,
 LYMPHOMAS (0354)
 IMMUNE LYMPHOID CELL, MURINE LYMPHOMA,
 MACROPHAGE (0725)
 IMMUNE RESPONSE, LYMPHOCYTE PROLIFERA-
 TION, LYMPHOPROLIFERATIVE DISEASE,
 REVIEW (0391)*
 IMMUNIZATION, TUMORIGENESIS INHIBITION
 SV40 (0671)
 IMMUNOCOMPETENCE, IMMUNOTHERAPY, HUMAN
 MELANOMAS AND SARCOMAS (0704)
 IMMUNOCYTE CLONAL EVOLUTION, AUTO-
 IMMUNE DISEASE, LYMPHOSARCOMA (0719)
 IMMUNOHEMOLYTIC ANEMIA, YOSHIDA
 SARCOMA CELLS, PENETRATION OF ANTI-
 TUMOR ANTIBODIES (0709)
 IMMUNOLOGICAL SURVEILLANCE (0355)
 IMMUNOPATHOLOGICAL PROFILE, TUMOR
 PROFILE, MOUSE STRAINS (0393)*
 IMMUNOSUPPRESSIVE DRUGS, RENAL TRANS-
 PLANTATION, CERVICAL DYSPLASIA
 (0693)
 IMMUNOSUPPRESSIVE THERAPY, MAMMARY
 ADENOCARCINOMA (0695)
 LYMPHO-EPITHELIAL THYMOMA, ORGAN
 TRANSPLANT, MAN (0360)
 MAMMARY GLAND, CARCINOMA, RAT,
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 (0454)
 MYELOMA, GAMMA A PROTEIN (0715)
 SERUM ANTIBODIES, INFECTIOUS MONO-
 NUCLEOSIS, EPSTEIN-BARR VIRUS
 (0577)
 TUMOR-SPECIFIC TRANSPLANTATION ANTI-
 GEN, HUMAN, REVIEW (0358)
 UREA-EXTRACTABLE ANTIGENS, BENIGN AND

MALIGNANT TUMORS, NORMAL MOUSE
 EPIDERMIS (0726)
 IMMUNOPROLIFERATIVE DISEASE
 LYMPHOSARCOMA, PLASMOCYTOMA, HODGKIN'S
 DISEASE, IMMUNOGLOBULINS (0734)
 IMMUNOSUPPRESSION
 BURKITT'S LYMPHOMA, VIRUS (0687)*
 IMURAN, STEROIDS, EARLY THYMECTOMY,
 ANTI-LYMPHOCYTE SERUM, ONCOGENICITY,
 REVIEW (0357)
 INDUCTION
 INFECTIVITY, SV40, MITOMYCIN C, OTHER
 AGENTS (0660)
 INFECTIOUS MONONUCLEOSIS
 EPSTEIN-BARR VIRUS (0353)
 EPSTEIN-BARR VIRUS, ANTIBODIES (0577)
 INFECTIVITY
 RAT VIRUSES, HEMAGGLUTINATION-INHIBI-
 TION (0559)
 INSULIN
 MAMMARY CARCINOMA, DIMETHYLBENZ(A)
 ANTHRACENE, RAT (0450)
 INTERCALATION
 POLYADENYLIC ACID, POLYCYCLIC HYDRO-
 CARBONS (0410)
 INTERFERON
 INTERFEROGEN, MURINE LEUKEMIA VIRUS,
 CROSS IMMUNIZATION (0595)
 MORTALITY, HARVEY MURINE SARCOMA VIRUS
 (0639)
 3T3 CELL CULTURE, POLYOMA VIRUS,
 TEMPERATURE-SENSITIVE POLYOMA MUTANT
 ONA (0678)
 INTESTINE, LARGE
 CARCINOMA, ADENOMATOUS POLYPS, SOUTH
 AFRICAN BANTU (0759)
 INTESTINE, SMALL
 HYPERPLASIA, HYPERTHYROIDISM, RAT
 (0740)
 IODINE
 RADIOACTIVE, BOMB FALLOUT, THYROID
 NEOPLASIA (0529)
 ISONICOTINIC ACID HYDRAZIDE
 TREATED WATER CONSUMPTION (0513)*
 JAW
 PAROSTEAL SARCOMA, OSTEOGENIC SARCOMA
 (0535)
 JEJUNUM
 MUCOSAL CRYPT CELLS, CELL SURVIVAL AND
 REPAIR, X-RAY AND NEUTRON IRRADI-
 ATION (0524)
 KIDNEY
 EPITHELIAL HYPERPLASIA, DIMETHYL-
 NITROSAMINE, TRANSPLACENTAL EFFECT,
 MOUSE (0477)
 MOUSE, GAS PHASE OF CIGARETTE SMOKE,
 CYTOCHEMISTRY (0501)
 MOUSE, POLYOMA VIRUS, DNA SYNTHESIS,
 T-ANTIGEN (0676)
 RIOPELLE'S TUMOR, HISTOGENESIS, REVIEW
 (0371)
 SV40 VIRUS, THYMIDINE KINASE, HAMSTER
 (0667)
 THOROTRAST, TUMORS (0366)
 TUMORS, MAMMARY GLAND TUMORS, MOUSE
 (0811)
 KINETICS
 CELL POPULATION, CAPILLARY ENDOTHELIAL
 CELLS, MOUSE MAMMARY TUMOR (0762)
 TUMOR SPECTRUM, URETHAN, AGE (0492)
 LEUKOCYTE

CHROMOSOME ABERRATIONS, X-IRRADIATION
 THERAPY, IN UTERO (0538)
 LEUKOCYTIC ZINC CONTENT, SKIN NEO-
 PLASIA (0787)
 PHENOTYPE, HODGKIN'S DISEASE, HL-A
 ANTIGEN (0717)
 LEUKEMIA
 ACUTE, OCCUPATIONAL EXPOSURE, CHLOR
 PHENOTHANE, BENZENE HEXACHLORIDE
 (0509)
 ACUTE LYMPHOCYTIC, FAMILIAL AGGREGA-
 TION (0796)
 ACUTE MYELOGENOUS, CYTOSTATIC TREAT-
 MENT, METASTASIZING OVARIAN
 CARCINOMA (0506)
 ACUTE MYELOGENOUS, PHI CHROMOSOME,
 ANEUPLOIDY (0798)
 ACUTE MYELOID, FRIEND VIRUS, EHRLICH
 ASCITES TUMOR, POLIOVIRUS, ECHOVI-
 RNA (0572)
 ACUTE MYELOID, RAPID BONE GROWTH,
 ADOLESCENCE (0375)
 ACUTE MYELOMONOCYTIC, MELPHALAN
 THERAPY, MULTIPLE MYELOMA (0507)
 AGE DEPENDENT VARIATION, RH NEGATIVE
 (0801)
 BLAST CELL, IGA PARAPROTEINEMIA, BE-
 JONES PROTEIN (0713)
 BONE MARROW CELL, PERIPHERAL BLOOD
 CELL, HUMAN (0779)
 CELL-FREE ORGAN EXTRACTS, MURINE
 MYELOID LEUKEMIA (0605)
 CHROMOSOMAL ABNORMALITY, HUMAN,
 HEMATOLOGICAL DISORDER (0800)
 CHRONIC LYMPHATIC, ABNORMAL PHOSPHO-
 GLUCOMUTASE ISOZYME (0794)
 CHRONIC MYELOID, CYTOGENETICS AND
 CARCINOGENESIS, PHILADELPHIA
 CHROMOSOME (0344)
 DETECTION, COMPLEMENT BINDING, VIRUS
 (0711)
 DIABETES, DNA SYNTHESIS, GLUCOSE
 METABOLISM (0775)
 DOMESTIC ANIMALS, VIRAL ETIOLOGY,
 REVIEW (0389)*
 EMBRYO CELL CULTURE, THYMUS CELL
 CULTURE, MOUSE (0599)
 EPSTEIN-BARR VIRUS, HUMAN EMBRYONIC
 CELL LINE (0570)
 FRIEND VIRUS, ERYTHROID DIFFERENTIA-
 TION (0603)
 GENETIC FACTORY, DERMATOGLYPHIC
 PATTERNS (0363)
 GENETIC IMPLICATION, TWIN, HUMAN
 (0364)
 HEMATOPOETIC CANCER, DEATH RATES,
 EPIDEMIOLOGY (0761)
 HL-A ANTIGEN FREQUENCIES (0714)
 IMMUNOFLOURESCENCE, PARABLASTS,
 CHILDREN, CONTACT PERSONS (0712)
 LEUKEMOGENESIS, AEROSOL EXPOSURE,
 VIRUS, RAUSCHER MURINE LEUKEMIA
 VIRUS (0608)
 LOW-LEUKEMIC STRAIN MICE, MURINE
 LEUKEMIA VIRUS, ANTIGEN (0596)
 LYMPHOBLASTS, TRANSFER RNA SPECIES,
 AMINOACYLATION (0790)
 LYMPHOMA, VIRUS-LIKE PARTICLES, HUMAN
 (0569)
 LYMPHOSARCOMA, VIRUS PARTICLES (055

N-(4-(5-NITRO-2-FURYL)-2-THIAZOLYL) ACETAMIDE, STOMACH NEOPLASM (0417)

ONCOGENIC VIRUSES, PRECIPITATING FACTORS (0351)

PAPOVA VIRUS, HAMSTER, LIVER, THYMUS (0672)

RADIATION, THERAPEUTIC DOSE (0370)

RNA, DNA POLYMERASE (0792)

SARCOMA VIRUS, C-TYPE MOUSE MAMMARY TUMOR VIRUS, B-TYPE POLYMERASE (0589)

VIRUS, MOUSE SPLEEN, WHOLE BODY IRRADIATION (0592)

IP

MUCOSA, CANCER, 7,12-DIMETHYLBENZ(A) ANTHRACENE, HAMSTER (0483)

IPOPROTEIN

SERUM, HIGH-DENSITY LEVEL (0785)

LIVER

ANTIGENS, HEPATOMA, DIMETHYLAMINO-AZOBENZENE, DIETHYLAMINO-AZOBENZENE (0434)

BENZOPYRENE, CARBON MONOXIDE, RAT (0459)

BIOSYNTHESIS OF BILE ACIDS, METHYL-CHOLANTHRENE (0462)

CARCINOMA, RAT, N-HYDROXY-N-2-FLUORENYLACETAMIDE (0409)

CHICK EMBRYOS, PALMOTOXINS, AFLATOXIN (0425)

CYTOCHROME P-450, 3-METHYLCHOLANTHRENE PHENOBARBITAL, RAT (0464)

DIMETHYLAMINO-AZOBENZENE, CARCINOGENESIS, NAPHTHYLSISOTHIOCYANATE INHIBITION, RAT (0433)

FERRITIN, CARCINOGENS, RAT (0475)

HEPATO CARCINOMA, 3-METHYL-4-DIMETHYLAMINO-AZOBENZENE, RAT (0429)

HEPATOCELLULAR CARCINOMA, HEPATITIS-ASSOCIATED ANTIGEN (0723)

HEPATOCELLULAR CARCINOMA, STERIGMATOCYSTIN, RATS (0402)

HEPATOMA, BETA-PROPIOLACTONE, TUMOR INDUCTION (0399)

HYPERPLASTIC NODULE, RAT, 3-METHYL-4-DIMETHYLAMINO-AZOBENZENE, 2-FLUORENYL ACETAMIDE, DL-ETHIONINE (0430)

IRRADIATION, AMINO ACIDS, PERFUSION (0537)

KUPFFER CELL, BILE DUCT EPITHELIUM, HYPERPLASIA, AFLATOXIN B1, HAMSTER (0517)

LUNG, CARCINOMA, HYDRAZINE SULFATE, MOUSE, ISONIAZIDE METABOLISM, MAN (0415)

MAMMARY TUMOR VIRUS, BRAIN GR MOUSE (0629)

3-METHYLCHOLANTHRENE, DIMETHYLNITROSAMINE O-METHYLASE INHIBITION, RAT (0466)

NUCLEIC ACID METHYLATION, DIMETHYLNITROSAMINE, METABOLISM (0473)

POLYRIBOSOMES, X-IRRADIATION, HORMONE, RAT (0544)

PRIMARY CANCER, AUSTRALIA ANTIGEN (0724)

PROTEIN ADDUCT, N-HYDROXY-2-FLUORENYLACETAMIDE, RAT (0407)

RHESUS MONKEY, DIETARY AFLATOXINS (0426)

SYNCARCINOGENESIS, NITROSAMINES, RATS (0435)

THOROTRAST, TUMORS (0366)

LUNG

ADENOMA, CARCINOMA, HYDRAZINE SULFATE, GONADECTOMY, MOUSE (0414)

ADENOMA, LEUKEMIA, N-DIAZOACETYLGLYCINAMIDE, N-DIAZOACETYLGLYCINE HYDRAZIDE, MOUSE (0401)

ALVEOLAR CELL CARCINOMA, DNA, ALVEOLAR MACROPHAGE (0736)

ALVEOLAR EPITHELIAL CELLS, 4-NITROQUINOLINE 1-OXIDE, NUCLEOLAR ALTERATIONS (0491)

BRONCHIAL CARCINOMA, GONADOTROPHIN SECRETION, TROPHOBLASTIC DIFFERENTIATION (0774)

BRONCHIAL CARCINOMA, HYDROCARBONS, CARCINOGENS, AIR POLLUTION (0461)

BRONCHIAL SECRETION, CARCINOMA, TOBACCO SMOKE (0750)

BRONCHOALVEOLAR CANCER, OVINE PULMONARY ADENOMATOSIS, NEOPLASTIC FEATURES (0820)

BRONCHOGENIC CARCINOMA, HISTOPATHOLOGY GROWTH RATE, METASTASIS (0764)

CANCER, CYCLAMATE, HEPATOMA, MOUSE, REVIEW (0378)

CANCER, HIGH-RISK GROUPS, CIGARETTE SMOKING (0751)

CANCER, HISTOLOGY, MORPHOLOGY (0829)

CANCER, INCIDENCE, AIR POLLUTION, SMOKING, ITALY (0383)

CANCER, INFLUENZA VIRUS, MICE, CELL METAPLASIA (0564)

CARCINOMA OF THE BRONCHUS, PLASMA GROWTH HORMONE, HYPERTROPHIC OSTEOARTHROPATHY (0773)

EMBRYONIC LUNG ORGAN, EXPLANT, MOUSE, GAS PHASE OF CIGARETTE SMOKE, CYTOCHEMISTRY (0501)

EPITHELIOMA, MEDIASTINAL LYMPHOMA, URETHAN, VIRUS PARTICLES, GERM-FREE MOUSE (0494)

HISTOLOGY, N-NITROSO-N-METHYLURETHANE, ALKALINE PHOSPHATASE, MOUSE (0486)

LIVER, CARCINOMA, HYDRAZINE SULFATE, MOUSE, ISONIAZIDE METABOLISM, MAN (0415)

NEOPLASMS, CHOLESTEROL, LIPID, DIET, PITUITARY CHANGES (0397)

NICKEL CARBONYL GAS (0510)

SURFACE ACTIVITY, LECITHIN METABOLISM, EFFECTS OF RADIATION (0542)

URETHAN, PHENOBARBITAL, MOUSE (0493)

LYMPH

NODE, SARCOMA, 3-METHYLCHOLANTHRENE, MOUSE (0471)

NODE, URIDINE UPTAKE, DIMETHYLBENZ(A) ANTHRACENE, ANTI-LYMPHOCYTE SERUM (0456)

LYMPHATICS

MALIGNANT MELANOMA, MICROMETASTASES, PRIMARY TUMOR (0778)

LYMPHOCYTE

BLASTOGENESIS, MUTAGENESIS, AORIAMYCIN HUMAN (0699)

BLASTOGENESIS, PROTEIN ACCUMULATION, PHYTOHEMAGGLUTININ STIMULATION (0697)

CYCLAMATE, CHROMOSOME ABERRATION (0418)
 HOST RESPONSE, CHILDREN, HODGKIN'S DISEASE (0756)
 PHYTOHEMAGGLUTININ, FOLATE UPTAKE, HUMAN (0701)
 PHYTOHEMAGGLUTININ CONSUMPTION, HODGKIN'S DISEASE (0733)
 PHYTOHEMAGGLUTININ-TRANSFORMED, MEGALOBlastic ANEMIA, MORPHOLOGY, DNA SYNTHESIS, HUMAN (0698)
 PRIMARY MELANOMA, METASTASIS (0722)
 PROLIFERATION, IMMUNE RESPONSE, LYMPHOPROLIFERATIVE DISEASE, REVIEW (0391)*
 THYMIC, SPLEEN, LACTIC DEHYDROGENASE PASSANGER VIRUS, RAUSCHER LEUKEMIA VIRUS (0609)
 TRANSFORMATION, CYCLIC AMP, PHYTOHEMAGGLUTININ (0702)
 TRANSFORMATION, DNA SYNTHESIS, ALPHA-AMINO-P-TOLUENESULFONAMIDE, HUMAN (0508)
 TRANSFORMATION, PHYTOHEMAGGLUTININ, DNA POLYMERASE, REPLICATION (0703)
 LYMPHOMA
 DOUBLE-STRAND DNA BREAKS, X-IRRADIATION, MURINE (0523)
 FELINE, C-TYPE VIRUS PARTICLES, ENVELOPE SPIKES (0588)
 IMMUNOLOGICAL FACTOR (0354)
 MEDIASTINUM, URETHAN, PARTICLES, VIRUS (0495)
 MOLONEY LEUKEMOGENIC VIRUS, PLASMONIUM BERGHEI VOELT (0600)
 MORPHOLOGY, BURKITT TUMOR, EPSTEIN-BARR VIRUS (0575)
 MURINE, MACROPHAGE, IMMUNE LYMPHOID CELLS (0725)
 ROWSON-PARR VIRUS, MICE (0610)
 LYMPHOPROLIFERATIVE DISEASE
 IMMUNE RESPONSE, LYMPHOCYTE PROLIFERATION, REVIEW (0391)*
 LYMPHOSARCOMA
 AFFECTED SIBLINGS, CYTOGENIC ABNORMALITY (0694)
 BURKITT'S LYMPHOMA, MALARIA (0689)*
 CATTLE, BOVINE SYNCYTIAL VIRUS, MORPHOLOGICAL VARIANT (0563)
 IMMUNOCYTE CLONAL EVOLUTION, AUTO-IMMUNE DISEASE (0719)
 LEUKEMIA VIRUS PARTICLES, MORPHOLOGY AND DISTRIBUTION, VIRUS (0550)
 RABBIT, GENETICS AND PATHOLOGY (0802)
 TOAD, COCKROACH VECTOR (0565)
 LYSINE
 5-N-METHYLATED, ERLICH SUBCUTANEOUS CARCINOMA, GROWTH-PROMOTING EFFECTS (0816)
 LYSOPINE
 OCTOPINE, PLANT TUMORIGENESIS PROMOTERS (0404)
 MACROPHAGE
 ALVEOLAR CELL CARCINOMA, DNA CONTENT (0736)
 IMMUNE LYMPHOID CELLS, MURINE LYMPHOMA (0725)
 MALARIA
 BURKITT'S LYMPHOMA, LYMPHOSARCOMA (0689)*

COCARCINOGEN, BURKITT'S LYMPHOMA (0690)*
 MALIGNANT MELANOMA INDUCTION
 URETHAN (0497)
 MALIGNOMA
 RADIATION, THERAPEUTIC DOSE (0370)
 MAMMARY GLAND
 ADENOCARCINOMA, IMMUNOSUPPRESSIVE THERAPY (0695)
 ADENOCARCINOMA, TESTOSTERONE, ESTROGEN (0448)
 ADENOCARCINOMA, THYMIC LYMPHOSARCOMA
 4(5)-(3,3-DIMETHYL-1-TRIAZENO)IMIDAZOLE-5(4)-CARBOXAMIDE (0423)
 CARCINOGENESIS INHIBITION, PROLACTIN (0440)
 CARCINOMA, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, IMMUNOLOGY, RAT (0454)
 CARCINOMA, MAMMARY TUMOR VIRUS (0633)
 CARCINOMA, RAT, DIMETHYLBENZ(A)-ANTHRACENE, INSULIN (0450)
 CARCINOMA, RAT, 9,10-DIMETHYL-1,2-BENZANTHRACENE (0442)
 CARCINOMA, RNA-TYPE VIRUSES, MONKEY (0626)
 COMEDOCARCINOMA, HISTOLOGICAL EXAMINATION, ORAL CONTRACEPTIVE (0505)
 7,12-DIMETHYLBENZ(A)ANTHRACENE, HORMONAL ANTITUMOR AGENTS, RAT (0457)
 KIDNEY, TUMORS, MOUSE (0811)
 SPONTANEOUS, ADENOCARCINOMA, VIRUS PARTICLES (0630)
 STRAIN DIFFERENCES, HORMONE, LOBULOALVEOLAR DIFFERENTIATION, MOUSE (0769)
 TUMOR, CELL POPULATION KINETICS, CAPILLARY ENDOTHELIAL CELLS (0762)
 TUMOR, HYPOTHALAMIC LESION, PROLACTIN (0770)
 TUMOR, SPLENECTOMY, THYMECTOMY (0621)
 TUMOR, VIRUS PARTICLES, HEMATOPOIETIC ORGANS, THYMUS, EPIDIDYMI, MOUSE (0632)
 TUMOR CELLS, PROTEIN SYNTHESIS, LABELED METHIONINE INCORPORATION, MOUSE (0793)
 MAREK'S DISEASE
 SENDAI VIRUS (0581)
 MEDIASTINUM
 LYMPHOMA, LUNG EPITHELIOMA, URETHAN, VIRUS PARTICLES, GERM-FREE MOUSE (0494)
 LYMPHOMA, URETHAN INDUCED, VIRUS-LIKE PARTICLES (0495)
 MELANIN
 SYNTHESIS, PROLIFERATION, MOUSE PIGMENT CELL (0812)
 MELANOMA
 HUMAN, CHANGES DURING MITOSIS, GOLGI APPARATUS (0786)
 LYMPHATICS, MALIGNANT, MICROMETASTASIS
 PRIMARY TUMOR (0778)
 MALIGNANT, CONJUNCTIVA (0749)
 PRIMARY, METASTATIC, LYMPHOCYTIC REACTION (0722)
 RADIATION THERAPY, FACE AND LIP (0511)
 SARCOMAS, IMMUNOCOMPETENCE, IMMUNO-

THERAPY, HUMAN (0704)
 SKIN GENETICS, MAN (0830)*
 TUMOR EMBOLI, METASTASIS, DISTRIBUTION
 OF LABELED TUMORS (0822)
 PHALAN
 MULTIPLE MYELOMA, ACUTE MYELOMONOCYTIC
 LEUKEMIA (0507)
 BRANE
 AGGLUTINATION, POLYOMA VIRUS, NON-
 TRANSFORMING MUTANT (0680)
 CHICK CHORIOALLANTOIC, ROUS SARCOMA
 VIRUS, URIDINE METABOLISM (0643)
 TRANSFORMED CELL, SURFACE, CARBO-
 HYDRATE LOCATION (0708)
 ABOLISM
 CANCER PATIENTS, HORMONAL ABNORMAL-
 ITIES, DISCRIMINANT FUNCTION (0372)
 GLUCOSE, LEUKEMIA AND DIABETES, DNA
 SYNTHESIS (0775)
 PROTEIN, MAMMARY GLAND TUMOR,
 METHIONINE INCORPORATION, MOUSE
 (0793)
 URIDINE, CHICK CHORIOALLANTOIC MEM-
 BRANE, ROUS SARCOMA VIRUS (0643)
 APLASIA
 LUNG CANCER, MICE, INFLUENZA VIRUS
 (0564)
 ASTASIS
 DISTRIBUTION OF LABELED TUMORS,
 MELANOMA TUMOR EMBOLI (0822)
 MELANOMA, PRIMARY MELANOMA, LYMPHO-
 CYTIC REACTION (0722)
 MICROMETASTASES, LYMPHATICS, MELANOMA,
 PRIMARY TUMOR (0778)
 OVARIAN CARCINOMA, ACUTE MYELOGENOUS
 LEUKEMIA, CYTOSTATIC TREATMENT
 (0506)
 PATTERN, ADENOCARCINOMA, THYROID,
 HUMAN (0823)
 SARCOMA, IMMUNIZATION, RAT,
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 (0455)
 WALKER'S CARCINOMA, GASTRIC WALL, RAT
 (0763)
 HANESULPHONOXY-ALKANE
 METHYL METHANESULPHONATE, ETHYL
 METHANESULPHONATE, ISOPROPYL
 METHANESULPHONATE, BLOOD, SPLEEN
 COLONY (0413)
 MIONINE SULFOXIMINE
 X-IRRADIATION, BONE MARROW CELL COUNTS
 (0405)
 NYLAZOXYMETHANOL-ACETATE
 DNA, LIVER (0427)
 ETHYLCHOLANTHRENE
 AGE DEPENDENCE, CARCINOGENESIS, MOUSE,
 RAT (0436)
 BENIGN AND MALIGNANT TUMORS, NORMAL
 MOUSE EPIDERMIS, UREA-EXTRACTABLE
 ANTIGENS (0726)
 BIOSYNTHESIS OF BILE ACIDS (0462)
 CHROMATIN, RAT LIVER NUCLEI, RNA
 SYNTHESIS (0463)
 CYTOCHROME P-450, PHENOBARBITAL, RAT
 (0464)
 DIMETHYLNITROSOAMINE DEMETHYLASE,
 CARBOHYDRATE REPRESSION (0474)
 GLUTAMATE, SUCCINATE, LACTATE,
 ISOCITRATE, GLUCOSE-6-PHOSPHATE
 DEHYDROGENASE, MOUSE (0469)

MURINE SARCOMAS, COMMON ANTIGENICI-
 TIES (0468)
 RAT LIVER, DIMETHYLNITROSOAMINE
 DEMETHYLASE INHIBITION (0466)
 SARCOMA, LYMPH NODE CELL, MOUSE (0471)
 SKIN SARCOMATA, OXYGEN CONSUMPTION
 (0465)
 SKIN TUMORS, RAT (0470)
 3-METHYL-4-DIMETHYLAMINOAZOBENZENE
 AMINOAZO DYE-BOUND PROTEIN (0431)
 HEPATO CARCINOMA, A5-300, RAT (0429)
 HYPERPLASTIC NODULE, LIVER, RAT (0430)
 METHYLETHYLNITROSOAMINE
 CARCINOGENIC MECHANISM, ELECTRONIC
 CONSIDERATIONS (0472)
 N-METHYL-N,N-NITRO-N-NITROSOGUANIDINE
 EMBRYONIC LUNG CELL CULTURE, HUMAN,
 CELL CYCLE, CHROMOSOME (0484)
 EXCISION OF METHYLATION PRODUCTS,
 E. COLI DNA (0485)
 N-METHYL-N-NITROSO-N'-ACETYLUREA
 PYLORUS, GASTRIC ADENOMA, RAT (0483)
 MINERAL OIL
 PLASMA CELL GRANULOMA, VIRUS-LIKE
 PARTICLES (0396)
 MITOMYCIN C
 SV40, OTHER AGENTS (0660)
 TRANSFORMED MOUSE KIDNEY CELLS,
 5-BROMODEOXYURIDINE, GENETIC CHANGE
 (0664)
 MITOSIS
 AROMATIC AMINES, YEAST CELLS, GENETIC
 ACTIVITY (0412)
 CELL CULTURES IN VITRO, BURKITT'S
 LYMPHOMA, PHYTOHEMAGGLUTININ (0730)
 CYCLIC AMP, BONE MARROW, THYMUS, RAT
 (0818)
 HUMAN MELANOMA, GOLGI APPARATUS (0786)
 INHIBITION, CELL CULTURE, 6,4-BENZ-
 PYRENE, LUNG, RAT (0460)
 N-METHYL-N,N-NITRO-N-NITROSOGUANIDINE,
 EMBRYONIC LUNG CELL CULTURE, HUMAN
 (0484)
 MORBIDITY
 PULMONARY CANCER INCIDENCE, SARDINIA
 (0766)*
 MORTALITY
 HARVEY MURINE SARCOMA VIRUS, INTER-
 FERON (0639)
 MOUTH
 ORAL MUCOSA, OENTURE IRRITATION,
 INFLAMMATORY PAPILLARY HYPERPLASIA
 (0737)
 MUTAGENESIS
 ARABIDOPSIS PLANT, HEAVY ION IRRADIA-
 TION (0539)
 HUMAN LYMPHOCYTES, BLASTOGENESIS IN
 HUMAN LYMPHOCYTES, ADRIAMYCIN (0699)
 MUTAGENICITY
 CARCINOGEN, BACTERIOPHAGE T4 (0400)
 MUTATION
 CHROMOSOME, DIMETHYLBENZANTHRACENES,
 DROSOPHILA MELANOGASTER (0439)
 MYCOBACTERIUM BOVIS
 GUINEA PIG ASCITES TUMOR, INHIBITION
 OF TUMOR GROWTH (0727)
 MYCOPLASMA
 CHROMOSOME ABERRATIONS, SV40 (0665)
 MYELOMA
 CHROMOSOMAL ABNORMALITY, HUMAN (0797)

CHROMOSOME NUMBER ALTERATION, MSPC-1
TUMOR, MOUSE (0716)
GAMMA A PROTEIN (0715)
MULTIPLE, ACUTE MYELOMONOCYTIC LEU-
KEMIA, MELPHALAN THERAPY (0507)
PLASMA CELL, IMMUNOGLOBULIN BIOSYNTHESIS (0720)
MYELOPROLIFERATIVE DISEASE
C-GROUP CHROMOSOME, LEUKEMIC REACTION
(0799)
NOSOLOGY, PHILADELPHIA CHROMOSOME
(0359)
NAPHTHYL ISOTHIOCYANATE
INHIBITION, DIMETHYLAMINOAZOBENZENE,
LIVER, RAT (0433)
NASOPHARYNX
CARCINOMA, EPSTEIN-BARR VIRUS, SURFACE
ANTIGEN (0579)
CARCINOMA, HERPES-TYPE VIRUS, LYMPHO-
BLASTOID TRANSFORMATION (0625)
CARCINOMA, MEMBRANE ANTIGEN, EPSTEIN-
BARR VIRUS, BURKITT'S LYMPHOMA
(0578)
NEOPLASM
MALIGNANT, EPIDEMIOLOGY, CHILD, CANADA
(0755)
RNA VIRUSES, DNA VIRUSES, REVIEW
(0381)*
TUMOR PROFILE, IMMUNOPATHOLOGICAL
PROFILE, MOUSE STRAIN DIFFERENCES,
REVIEW (0393)*
NERVOUS SYSTEM
TUMORS, CHILDREN, CHROMOSOMAL
CHARACTERISTICS (0804)
NEUROBLASTOMA
ACETYLCHOLINESTERASE, MOUSE (0783)
CELL-FREE EXTRACT, TUMOR INDUCTION
(0567)
NICKEL CARBONYL
GAS, EFFECTS OF ACCIDENTAL EXPOSURE
(0510)
NICOTINE
GASTRIC SECRETION, MUCOSAL SEROTONIN
LEVEL, RAT, ATROPINE (0502)
N-(4-(5-NITRO-2-FURYL)-2-THIAZOLYL)
ACETAMIDE
STOMACH NEOPLASM, LEUKEMIA (0417)
4-NITROQUINOLINE-1-OXIDE
ALVEOLAR EPITHELIAL CELLS, NUCLEOLAR
ALTERATIONS (0491)
BACTERIOPHAGE, BACTERIAL MUTANTS
(0489)
MODE OF INCORPORATION, BINDING (0490)
NITROSAMINE DERIVATIVES
RATS, HEPATOCELLULAR CARCINOMA (0435)
N-NITROSOHEXAMETHYLENEMINE
OROPHARYNGEAL TUMOR, FACIAL TUMOR,
MOUSE, EPITHELIUM (0479)
N-NITROSO-N-METHYLANILINE
GASTROINTESTINAL TRACT, PAPILLOMA,
CARCINOMA (0476)
N-NITROSO-N-METHYLCYCLOHEXYLAMINE
GASTROINTESTINAL TRACT, PAPILLOMA,
CARCINOMA (0476)
N-NITROSO-N-METHYLUREA
RESPIRATORY TRACT, EPIDERMOID
CARCINOMA, HAMSTER (0482)
N-NITROSO-N-METHYLURETHAN
LUNG HISTOLOGY, ALKALINE PHOSPHATASE,
MOUSE (0486)

N-NITROSOMORPHOLINE
RIBOSOMAL FERRITIN, RAT LIVER (047)
N-NITROSOPENTAMETHYLENEMINE
OROPHARYNGEAL TUMOR, FACIAL TUMOR,
MOUSE, EPITHELIUM (0479)
NOSE
NASAL PAPILLOMATOSIS, HISTOLOGY, V
ETIOLOGY (0373)
NOSOLOGY
PHILADELPHIA CHROMOSOME, MYELOPRO-
LIFERATIVE DISEASES (0359)
NUCLEIC ACID
DNA, RNA, COMPLEMENTATION (0554)
DNA, RNA, POLYMERASE, ENDONUCLEASE
ROUS SARCOMA VIRUS (0647)
DNA, RNA, POLYMERASE, ONCOGENIC VI
(0553)
INHIBITION, HEPATOMA, PREDNISOLONE
PHYTOHEMAGGLUTININ (0696)
METHYLATION, CHEMICAL CARCINOGEN,
DIMETHYLNITROSAMINE, METABOLISM
(0473)
POLYRIBONOSINIC-POLYRIBOCYTIDYLIC
ACID, POLYOMA VIRUS, INHIBITION
ONCOGENESIS (0685)
RNA, DNA, POLYMERASE, AVIAN MYELOBL
TOSIS (0586)
RNA, DNA, POLYMERASE, ROUS SARCOMA
VIRUS (0651)
SYNTHESIS, SHOPE FIBROMA VIRUS
INFECTION, VIRUS, FOCUS FORMATION
(0657)
NUTRITION
HIGH-VOLUME FEEDING, OCULAR CARCINO
IN CATTLE (0780)
OCCUPATIONAL HAZARD
BENZENE HEXACHLORIDE, CHLOROPHENO-
THANE, ACUTE LEUKEMIA (0509)
LABORATORY WORKER, BLADDER CARCINO
CHEMICAL CARCINOGEN (0367)
OCTOPINE
PLANT TUMORIGENESIS PROMOTERS (040)
ODONTOLOGY
MIXED CALCIFIED ODONTOGENIC TUMORS
PATHOLOGY, CLINICAL PROFILE (037)
ORAL CONTRACEPTIVE
CHROMOSOME ABNORMALITIES (0503)
MAMMARY COMEDOCARCINOMA, HISTOLOGIC
EXAMINATION (0505)
SEQUENTIAL, CYTOLOGIC ABNORMALITIES
CARCINOMA IN SITU (0504)
OSTEOSARCOMA
MOLONEY VIRUS, RAT (0637)
OVARY
ASCITES TUMOR, SULFANILIC ACID-
CONJUGATED ANTIGENS, RAT (0732)
FAMILIAL OVARIAN CARCINOMA, PAPILLO
ADENOCARCINOMA, GENETIC PREDISPO
TION (0808)
8-OXYQUINOLINE
CARCINOGENICITY, MOUSE, RAT (0487)
PALMOTOXIN
EMBRYO LIVER, AFLATOXIN (0425)
PAROTID GLAND
MIXED TUMOR (0530)
PESTICIDES
ALDRIN, DIELDRIN, ENDRIN, TUMOR-
IGENICITY (0421)
PETROLEUM
PRODUCT, BAYOL F, PLASMACYTOMA IN

TION, ANTITHYMOCYTE SERUM (0691)
 ENOBARBITAL
 CYTOCHROME P-450, 3-METHYLCHOLANTHRENE
 RAT (0464)
 URETHAN CARCINOGENESIS, LUNG, MOUSE
 (0493)
 ENOL
 DERIVATIVES, STRUCTURE-ACTIVITY
 RELATIONS, HAMMETT-TAFT EQUATION,
 REVIEW (0347)
 ECHROMOCYTOMA
 FAMILIAL, MEDULLARY THYROID CARCINOMA,
 CALCITONIN ACTIVITY (0803)
 FAMILIAL VON HIPPEL-LINDAU'S DISEASE
 (0828)*
 ILADELPHIA CHROMOSOME
 NOSOLOGY, MYELOPROLIFERATIVE DISEASES
 (0359)
 ORBOL
 MYRISTATE ACETATE, INDUCED VASCULAR
 CHANGES (0398)
 TRITIUM LABELING TECHNIQUE, CROTON OIL
 (0516)*
 OTOCARCINOGENICITY
 AROMATIC HYDROCARBON, MECHANISM (0345)
 YTOHEMAGGLUTININ
 BURKITT'S LYMPHOMA, CELL CULTURES IN
 VITRO, MITOTIC INDEX (0730)
 CONSUMPTION, LYMPHOCYTES, HOOBKIN'S
 DISEASE (0733)
 DNA SYNTHESIS IN LYMPHOCYTES, EXTRA-
 CORPOREAL IRRADIATION OF BLOOD
 (0526)
 FOLATE UPTAKE, HUMAN LYMPHOCYTES
 (0701)
 HUMAN LYMPHOCYTE BLASTOGENESIS,
 PROTEIN ACCUMULATION (0697)
 LYMPHOCYTE TRANSFORMATION, CYCLIC AMP
 (0702)
 LYMPHOCYTE TRANSFORMATION, DNA POLY-
 MERASE, REPLICATION (0703)
 LYMPHOCYTES, HEME-SYNTHESIS, HEMA-
 TOPOIETIC HUMORAL FACTORS (0700)
 MEGALOBlastic ANEMIA, MORPHOLOGY,
 DNA SYNTHESIS (0698)
 RNA SYNTHESIS, DNA SYNTHESIS, HEPATOMA
 (0696)
 TUITARY
 CHOLESTEROL-RICH DIET, LIPID-RICH
 DIET, NEOPLASMS, LUNG (0397)
 CENTA
 TRANSPLACENTAL EFFECT, DIMETHYLNITRO-
 SAMINE, NEOPLASM (0477)
 ANT
 ARABIDOPSIS, HEAVY ION IRRADIATION,
 MUTAGENESIS (0539)
 POLYCYCLIC HYDROCARBONS, AIR
 POLLUTANTS, FOOD (0397)
 ANT TUMOR
 PROMOTER, OCTOPINE, LYSOPINE (0404)
 ASMA
 CELL TUMOR, FREUND'S ADJUVANT (0395)
 ASMA CELL
 MYELOMA, IMMUNOGLOBULIN BIOSYNTHESIS
 (0720)
 ASMACYTOMA
 ASCITES TUMOR JR-1, MOUSE (0824)
 FREUND'S ADJUVANT, MICE (0394)
 INDUCTION, ANTITHYMOCYTE SERUM,
 RAYONL-F (0691)

MURINE, CELL DIFFERENTIATION, IN VITRO
 (0819)
 SERUM PARAPROTEIN (0729)
 POLLUTION
 CHEMICAL CARCINOGENS, TERATOGEN
 (0518)*
 POLONIUM
 RADIOACTIVITY, TOBACCO SMOKE, REVIEW
 (0382)*
 POLYPS
 ADENOMATOUS, SOUTH AFRICAN BANTU,
 CARCINOMA OF THE LARGE BOWEL (0759)
 CERVIX, HYPERESTRINISM, ENDOMETRIAL
 HYPERPLASIA (0742)
 POLYRIBOSOME
 SPLEEN, RAUSCHER VIRUS, MOUSE (0607)
 PROLACTIN
 MAMMARY CARCINOGENESIS INHIBITION
 (0440)
 RAT MAMMARY TUMOR, HYPOTHALAMIC LESION
 (0770)
 PROLIFERATION
 DNA SYNTHESIS, CELL DENSITY, EPITHE-
 LIUM (0813)
 MELANIN SYNTHESIS, MOUSE PIGMENT CELL
 (0812)
 POPULATION DENSITY, NORMAL EMBRYO CELL
 CULTURES, ROUS SARCOMA VIRUS,
 POLYOMA VIRUS, SARCOMA 180 (0814)
 BETA-PROPIOLACTONE
 TUMOR INDUCTION, HEPATOMA (0399)
 PROSTATE
 BENIGN ADENOMA, NEOPLASTIC TRANSFORMA-
 TION, PREMALIGNANT CONDITION (0745)
 PROTEIN
 ACCUMULATION, PHYTOHEMAGGLUTININ
 STIMULATION, HUMAN LYMPHOCYTE
 BLASTOGENESIS (0697)
 AMINOAZO DYE, 3'-METHYL-4-OIMETHYL-
 AMINOAZOBENZENE (0431)
 BENICE JONES, IGA PARAPROTEINEMIA,
 BLAST CELL LEUKEMIA (0713)
 BINDING, COMPLEX FORMATION, CARBO-
 HYDRATES, CARCINOGENESIS (0348)
 ALPHA-FETO, DIGESTIVE TRACT, TUMOR
 SPECIFIC ANTIGENS (0362)
 METABOLISM, LABELED METHIONINE INCOR-
 PORATION, MAMMARY GLAND TUMOR, MOUSE
 (0793)
 PARAPROTEIN, A-TYPE VIRUS-LIKE
 PARTICLES, MURINE PLASMA CELL
 NEOPLASIA (0593)
 SERUM PARAPROTEIN, PLASMACYTOMA CELLS
 (0729)
 STRUCTURAL, ADENOVIRUS TYPE 2 VIRION,
 DEGRADATION PRODUCTS (0613)
 PSEUDOVIRUS
 DNA, MOUSE EMBRYO CELLS, POLYOMA
 (0683)
 12H-PYRIDO(2,3-A)THIENO(2,3-1)CARBAZOLE
 STRUCTURE-ACTIVITY RELATIONSHIP, MOUSE
 (0411)
 RADIATION
 ATOMIC BOMB IRRADIATION, CHILHOODO
 CANCER INCIDENCE, CANCER MORTALITY
 (0540)
 BETA-RADIATION, EXPERIMENTAL OSTEO-
 SARCOMA, FEMORAL METAPHYSIS, RAT
 (0543)
 BLOOD, DNA SYNTHESIS, LYMPHOCYTES,

PHYTOHEMAGGLUTININ (0526)
 BONE MARROW LYMPHOCYTES, SPLENIC
 LYMPHOCYTES, CYTOMETRIC STUDY (0534)
 BURN SCARS, BASAL CELL CARCINOMA
 (0531)
 COBALT 60, 3H-URIDINE IRRADIATION,
 CHROMOSOME ABERRATIONS (0521)
 FACE AND LIP, MELANOMA (0547)
 FISSION NEUTRON IRRADIATION, ADRENAL
 CARCINOMAS (0532)
 GAMMA-RADIATION, RETINA, DYSPLASIA,
 DOG (0525)
 GAMMA RAYS, FROG VIRUS 3, DNA
 REPLICATION (0522)
 HEAVY ION IRRADIATION, MUTAGENESIS,
 ARABIDOPSIS PLANT (0539)
 INJURY, BONE MARROW TRANSPLANTATION,
 SPLENECTOMY (0533)

 ISOLATED LIVER, AMINO ACIDS, PERFUSION
 ACTIVE TRANSPORT (0537)
 LECITHIN METABOLISM IN LUNG, SURFACE
 ACTIVITY OF LUNG (0542)
 LEUKEMIA, THERAPEUTIC DOSE, MALIGNOMA
 32 (0370)
 32 PHOSPHORUS, ULTRASTRUCTURE, OSTEO-
 SARCOMA (0548)
 PROTEIN-BOUND NEUTRAL HEXOSES, HYPATO-
 CYTIC ULTRASTRUCTURAL CHANGES (0546)
 RADIOACTIVE IODINE, THYROTOXICOSIS,
 IATROGENIC CANCER (0549)
 SEX CHROMATIN, ENDOMETRIAL CANCER
 (0810)
 THOROTRAST, TUMORS, LIVER, KIDNEYS
 (0366)
 TRANSFORMATION, IN VITRO, REVIEW
 (0390)*
 UV, PHOTOCHEMICAL LESION, MOUSE (0536)
 UV IRRADIATION, ENHANCEMENT OF VIRAL
 TRANSFORMATION (0663)
 UV IRRADIATION, SV40, SURVIVAL (0668)
 UV IRRADIATION, TRANSFORMING CAPACITY,
 AVIAN SARCOMA VIRUS (0640)
 UV LIGHT, CROTON OIL, ACETIC ACID,
 XYLENE, MOUSE (0545)
 VISIBLE LIGHT, AVIAN SARCOMA VIRUS,
 5-BROMOURACINE, CHICK EMBRYO FIBRO-
 BLAST (0641)
 WHOLE BODY IRRADIATION, SPLEEN
 LEUKEMOGENIC VIRUS, MOUSE (0592)
 X-IRRADIATION, GROSS LEUKEMIA VIRUS,
 LEUKEMOGENESIS, SYNERGISM (0604)
 X-IRRADIATION, HORMONES, LIVER,
 POLYRIOSOMES (0544)
 X-IRRADIATION IN UTERO, CHROMOSOME
 ABERRATIONS (0538)
 X-IRRADIATION, METHIONINE SULFOXIMINE,
 BONE MARROW CELL COUNTS (0405)
 X-IRRADIATION, MURINE LYMPHOMA CELLS,
 DOUBLE-STRAND DNA BREAKS (0523)
 X-RAY AND NEUTRON IRRADIATION, CELL
 SURVIVAL AND REPAIR, JEJUNAL MUCOSAL
 CRYPT CELLS (0524)
 RADIOACTIVITY
 FALLOUT, RADIOACTIVE IODINE, THYROID
 NEOPLASIA (0529)
 RESCUE
 PSEUDOTYPE SARCOMA, MURINE LEUKEMIA
 VIRUS, NEW ZEALAND BLACK MICE (0606)
 RESPIRATORY TRACT
 N-NITROSO-N-METHYLUREA, EPIDERMOID

CARCINOMA, HAMSTER (0482)
 RETINA
 DYSPLASIA, RADIATION, DOG (0525)
 RETINOBLASTOMA
 CHROMOSOMAL ABERRATIONS, KARYOTYPE
 ANALYSIS (0805)
 DEVELOPMENTAL ABNORMALITIES, OR--
 DR-- CHROMOSOME CONDITIONS (0800)
 RNA
 BENZ(A)PYRENE, TUMOR IMMUNITY TRAN-
 (0728)
 BONE, SARCOMA GROWTH, RAT (0817)
 N-HYDROXY-ACETYLYAMINOFLUORENE,
 POLYRIBONUCLEOTIDE BINDING (0406)
 LEUKEMIA, DNA POLYMERASE (0792)
 LOW MOLECULAR WEIGHT, 4S, ROUS SAR-
 VIRUS (0646)
 NEOPLASTIC TISSUE, GROWTH AND DIFF-
 ENTATION, TRANSFER RNA METHYLAS-
 ACTIVITY (0791)
 NUCLEAR SYNTHESIS, FRIEND VIRUS (0
 POLYINOSINIC ACID/POLYCYTIDYLIC AC-
 RNA, SKIN TUMOR, 7,12-DIMETHYLBE-
 (A)ANTHRACENE, MOUSE (0447)
 SELF-REPLICATING, LEUKEMIA, VIRUS
 (0572)
 SYNTHESIS, ACFTAMIOOFLUORENE
 DERIVATIVES, RADIOACTIVE PRECURS-
 INCORPORATION (0408)
 SYNTHESIS, BROMODEOXYURIDINE, ROUS
 SARCOMA VIRUS (0645)
 SYNTHESIS, 3-METHYLCHOLANTHRENE,
 CHROMATIN, RAT LIVER NUCLEI (046
 TRANSFER, LEUKEMIC LYMPHOBLASTS,
 AMINOACYLATION (0790)
 SARCOMA
 ADENOVIRUS TYPE 12, IMMUNOLOGY,
 HAMSTER (0618)
 AXILLARY REGION, 3,4-BENZPYRENE, M-
 (0467)
 BLOCKADE, ROUS SARCOMA VIRUS, RAT
 VIRUS VACCINE, CHICKEN (0652)
 GROWTH, BONE RNA, RAT (0817)
 MELANOMA, IMMUNOCOMPETENCE, IMMUNE
 THERAPY, HUMAN (0704)
 3-METHYLCHOLANTHRENE, LYMPH NODE (C
 MOUSE (0471)
 MURINE, ANTIGENICITIES, 3-METHYL-
 CHOLANTHRENE (0468)
 OSTEOSARCOMA, FEMORAL METAPHYSIS,
 RADIATION (0543)
 PAROSTEAL, OSTEOGENIC SARCOMA OF
 JAW (0535)
 POLYMERIZED N-NITROSO-2,2,4-TRIMET
 1,2-DIHYDROQUINOLINE, SURCUTANER
 TISSUE, RAT (0488)
 ROUS SARCOMA VIRUS, VOLE (0642)
 SCHMIDT-RUPPIN ROUS VIRUS, THYMUS

 CHICKEN (0656)
 SKELETAL, ANTISARCOMA ANTIBODY,
 IMMUNITY (0710)
 TRANSPLANTATION, IMMUNITY, YEAST,
 MOUSE (0705)
 TUMOR RECURRENCE, ROUS SARCOMA VI-
 GROWTH (0650)
 YOSHIDA SARCOMA CELLS, PENETRATION
 ANTI-TUMOR ANTIBODIES, IMMUNO-
 HEMOLYTIC ANEMIA (0709)
 SARDINIA

TUMOR MORBIDITY DATA, PULMONARY CANCER
INCIDENCE (0766)*

ISTOSOMIASIS

SEMATOBIUM, BLADDER, CARCINOMA
(0771)

UM

ANTILYMPHOCYTE, CHEMICAL CARCINOGEN,
DIMETHYLBENZ(A)ANTHRACENE, LYMPHATIC
URINE UPTAKE (0456)

ANTITHYMOCYTE, RAYOL-F, PLASMACYTOMA
INJECTION (0691)

SUSCEPTIBILITY, CIGARETTE SMOKING,
URINARY BLADDER CANCER (0511)

N

BURN SCARS, RADIATION THERAPY, BASAL
CELL CARCINOMAS (0531)

9,10-DIMETHYLBENZANTHRACENE, ARYL
HYDROCARBON HYDROXYLASE, 7,8-BENZO-
FLAVONE, MOUSE (0445)

7,12-DIMETHYLBENZ(A)ANTHRACENE, HAIR
FOLLICLE CYCLE, MOUSE (0443)

HODGKIN'S DISEASE, INVASION MECHANISM
(0821)

MELANOMA, GENETICS, MAN (0830)*

METHYLCHOLANTHRENE, GLUTAMATE, SUCCIN-
ATE, LACTATE, ISOCITRATE, GLUCOSE-6-
PHOSPHATE DEHYDROGENASES, MOUSE
(0469)

NEOPLASIA, LEUKOCYTIC ZINC CONTENT
(0787)

SARCOMA, OXYGEN CONSUMPTION, METHYL-
CHOLANTHRENE (0465)

TUMOR, 7,12-DIMETHYLBENZ(A)ANTHRACENE,
POLYINOSINIC ACID/POLYCYTIOLIC
ACID RNA, MOUSE (0447)

TUMOR, 3-METHYLCHOLANTHRENE,
4-DEIMTHYLAMINOSTILBENE, RAT (0470)

TUMOR, UV IRRADIATION, CROTON OIL,
ACETIC ACID, XYLENE (0545)

UM CYCLAMATE

CHOLESTEROL, CARCINOGENESIS EXPERIMENT
OESIGN (0512)*

EEN

FRIEND LEUKEMIA VIRUS, GUAROA VIRUS,
ENHANCEMENT (0602)

LACTIC DEHYDROGENASE PASSENGER VIRUS,
RAUSCHER LEUKEMIA VIRUS, THYMIC
LYMPHOCYTE (0609)

LEUKEMOGENIC VIRUS, MOUSE, WHOLE BODY
IRRADIATION (0592)

LYMPHOCYTES, IRRADIATED BONE MARROW
LYMPHOCYTES, CYTOMETRIC STUDY (0534)

LYMPHOID CELLS, INHIBITION OF TUMOR
GROWTH, ADENOVIRUS TYPE 12 (0617)

LYMPHOID TUMORS, ANTITHYMOCYTE SERUM,
POLYOMA VIRUS (0682)

POLYRIBOSOME, RAUSCHER VIRUS, MOUSE
(0607)

SPLENECTOMY, BONE MARROW TRANSPLANTA-
TION, RADIATION INJURY (0533)

SPLENECTOMY, THYMECTOMY, MAMMARY
TUMORIGENESIS (0628)

RIGHMOCYSTIN

HEPATOCELLULAR CARCINOMA, RATS (0402)

ROIO

7,12-DIMETHYLBENZ(A)ANTHRACENE,
CORTISONE ACETATE (0451)

SYNTHESIS, ADRENAL CARCINOMA, HUMAN
(0782)

STOMACH

ADENOMA, N-METHYL-N-NITROSO-N'-
ACETYLUREA, PYLORUS, RAT (0483)

CANCER, ANTIGENS, EMBRYONAL TISSUE,
MAN (0707)

CARCINOMA, GERMANY, MORTALITY,
DETECTION (0765)*

GASTRIC CARCINOMA, STOMACH SURGERY
(0528)

GASTRIC CARCINOMA, VITILIGO, ANEMIA
(0777)

GASTRIC SECRETION, MUCOSAL SEROTONIN
LEVEL, NICOTINE, ATROPINE (0502)

NEOPLASM, LEUKEMIA, N-(4-(5-NITRO-2-
FURYL)-2-THIAZOLYL)ACETAMIDE (0417)

STRUCTURE

ACTIVITY RELATIONSHIP, CARCINOGEN,
8,9-BENZO-GAMMA-CARBOLINE,
12H-PYR100(2,3-A)THIENO(2,3-1)CAR-
BAZOLE, MOUSE (0411)

ACTIVITY RELATIONSHIP, PHENOL COM-
POUNDS, HAMMETT-TAFT EQUATION,
REVIEW (0347)

SULFAMYLON

ALPHA-AMINO-P-TOLUENESULFONAMIDE,
LYMPHOCYTE TRANSFORMATION, DNA
SYNTHESIS, HUMAN (0508)

SYNDROME

CUSHING'S, HORMONAL TREATMENT,
CARCINOMA, BILATERAL HYPERPLASIA,
ADRENALECTOMY (0741)

SYNERGISM

LEUKEMOGENESIS, GROSS LEUKEMIA VIRUS,
X-IRRADIATION (0604)

LIVER, NITROSAMINES, RATS (0435)

TEMPERATURE

ASPERGILLUS FLAVUS, AFLATOXIN PRODUCE-
TION (0519)*

VIRAL REPLICATION, SV40, MUTANT (0666)

TERATOGENESIS

SMOKING, KLINEFELTER'S SYNDROME (0376)

TESTES

EMBRYONAL ADENOCARCINOMA, CHILDREN,
HISTOGENESIS (0746)

TESTOSTERONE

7,12-DIMETHYLBENZ(A)ANTHRACENE,
CASTRATED AND INTACT HAMSTERS
(0449)

MAMMARY ADENOCARCINOMA, ESTROGEN
(0448)

THIOACETAMIDE

RIBOSOMAL FERRITIN, RAT LIVER (0475)

THYMECTOMY

NEONATAL, ANTILYMPHOCYTE SERUM
THERAPY, IMMUNE DEFICIENCY,
ONCOGENICITY, REVIEW (0357)

THYMUS

CELL CULTURE, LEUKEMIA, MOUSE (0599)

CHICKEN, SARCOMA, SCHMIDT-RUPPIN ROUS
VIRUS (0656)

LEUKEMIA, HAMSTER, PAPOVA VIRUS (0672)

LYMPHOMA, CELL-FREE SUPERNATANTS,
GENETIC SUSCEPTIBILITY (0594)

LYMPHOMA, MURINE LEUKEMIA VIRUS,
ALKALINE PHOSPHATASE, RAT (0590)

LYMPHOSARCOMA, IMMUNOLOGY, ORGAN
TRANSPLANT, MAN (0360)

LYMPHOSARCOMA, MAMMARY ADENOCARCINOMA,
4(5)-(3,3-DIMETHYL-1-TRIAZENO)-
IMIDAZOLE-5(4)CARBOXYAMIDE (0423)

THYMECTOMY, MAMMARY TUMORIGENESIS,
 SPLENECTOMY (0628)
 THYROID
 ADENOCARCINOMA, METASTATIC PATTERN,
 HUMAN (0623)
 EPIDERMIOID CYST, ESTRADIOL, RAT,
 CASTRATION (0416)
 HYPERTHYROIDISM, HYPERPLASIA, SMALL
 INTESTINE, RAT (0740)
 MEDULLARY CARCINOMA, CALCITONIN
 ACTIVITY, FAMILIAL PHEOCHROMOCYTOMA
 (0803)
 NEOPLASIA, RADIOACTIVE IODINE EXPO-
 SURF, BOMB FALLOUT (0529)
 PAPILLARY CARCINOMA (0789)
 THYROTOXICOSIS
 IATROGENIC CANCER, RADIOACTIVE IODINE
 (0549)
 TOBACCO
 BRONCHIAL CARCINOMA, LOCALIZATION
 (0750)
 CIGARETTE SMOKING, HIGH-RISK GROUP,
 LUNG CANCER (0751)
 CIGARETTE SMOKING, URINARY BLADDER
 CANCER, SEX DIFFERENCE (0511)
 CONDENSATES, ESTERASE ACTIVITY AREA
 TEST, CARCINOGENICITY (0499)
 LUNG, KIDNEY, MOUSE (0501)
 RADIOACTIVE POLONIUM POTASSIUM,
 RADON, REVIEW (0382)*
 TERATOGENESIS, KLINEFELTER'S SYNDROME
 (0376)
 TWIN METHOD, CANCER INCIDENCE (0500)
 TOXICITY
 OILSEED PROTEINS, ANIMAL FEED AFLA-
 TOXIN, REVIEW (0387)*
 TRACHEA
 MUCOSA, PAPILLOMATA, DIETHYLNITROSO-
 AMINE, GOLDEN HAMSTER (0480)
 TRANSFORMATION
 AVIAN SARCOMA VIRUS, UV-IRRADIATION
 (0640)
 EMBRYONIC TISSUE CULTURES, ROUS
 SARCOMA VIRUS, GRAFT (0654)
 FUSIFORM CELL, ROUS SARCOMA VIRUS
 MUTANT (0649)
 HEMATOPOIETIC CELLS, AVIAN MYELOBLAS-
 TOSIS VIRUS (0583)
 LYMPHOCYTE, CYCLIC AMP (0702)
 MURINE LEUKEMIA VIRUS, MURINE SARCOMA
 VIRUS, VIRUS, NONPRODUCER VIRAL
 CLONES (0638)
 MURINE SARCOMA VIRUS, CELL MULTI-
 PPLICATION (0636)
 NEOPLASTIC, EMBRYONIC SYSTEMS,
 EPIGENETIC PROCESSES, REVIEW (0392)*
 NON-TRANSFORMING MUTANT, POLYOMA
 VIRUS, CELL MEMBRANE AGGLUTINATION
 (0680)
 OSTEOGENIC, FIBROBLASTS, XENOGENIC
 BONE TRANSPLANT (0738)
 POLYOMA VIRUS, VIRUS GENERATION,
 IN VITRO (0667)
 PREMALIGNANT CONDITION, BENIGN
 PROSTATIC ADENOMA (0745)
 SPONTANEOUS, TRANSFORMING AGENTS,
 ANIMAL CELL TRANSFORMATION IN VITRO,
 REVIEW (0390)*
 SUSCEPTIBILITY, VIRAL DNA, SV40 (0659)
 SV40 - ADENOVIRUS HYBRID, ANTIGEN

(0615)
 TUMOR-ANTIGEN PRODUCTION, SV40 (0615)
 TRANSMISSION
 MILK, GENETIC SUSCEPTIBILITY, VIRAL
 MAMMARY TUMOR VIRUS (0631)
 TRANSPORT
 ACTIVE, LIVER, PERFUSION, AMINO ACIDS
 (0537)
 TRAUMA
 STOMACH SURGERY, GASTRIC CARCINOMA
 (0528)
 TUMORIGENESIS
 AFLATOXINS, MYCOTOXINS, REVIEW (0615)
 AVIAN TUMOR VIRUS, STRAIN MC29, CHICKEN
 (0580)
 SV40, INHIBITION, IMMUNIZATION (0615)
 TYLOSIS
 CARCINOMA OF THE ESOPHAGUS, GENETIC
 LINKAGE (0776)
 ULTRASOUND
 HUMAN BLOOD CELL CULTURES, CHROMOSOME
 ABERRATIONS (0527)
 ULTRASTRUCTURE
 GOLGI APPARATUS, HUMAN MELANOMA,
 MITOSIS (0786)
 HEPATOCYTE, RADIATION, PROTEIN-ROUS
 NEUTRAL HEXOSSES (0546)
 LUNG CANCER: CLASSIFICATION, ELECTRON
 MICROSCOPE (0829)*
 MEDIASTINAL LYMPHOMA, LUNG EPITHELIAL
 URETHAN, GERM-FREE MOUSE (0494)
 NUCLEOCAPSID, AVIAN MYELOBLASTOSIS
 VIRUS (0587)
 OSTEOSARCOMA, 32 PHOSPHORUS (0548)
 TUMOR BUD CELL, SUPERFICIAL BASAL
 CELL CARCINOMA (0735)
 URETHAN
 ADRENAL TUMOR, ENDOCRINE LESION (0492)
 AGE, TUMOR SPECTRUM (0492)
 CARCINOGENESIS, PHENOBARRITAL, LUNG
 MOUSE (0493)
 CARCINOGENICITY, GUINEA PIGS (0493)
 MALIGNANT MELANOMA INDUCTION (0493)
 MEDIASTINAL LYMPHOMA, LUNG EPITHELIAL
 VIRUS PARTICLES, GERM-FREE MOUSE
 (0494)
 MEDIASTINAL LYMPHOMA, VIRUS-LIKE
 PARTICLES (0495)
 TUMOR PROFILE, PERINATAL AGE PERIOD
 (0496)
 UTERUS
 CERVIX, EPITHELIAL ATYPIA, COMBINATION
 CONTRACEPTIVES, HUMAN (0514)*
 ESTROGENS, POLYETHYLENE STRIPS, GUINEA
 PIG (0815)
 VACCINE
 TUMOR, ANTIGENIC "OTHERNESS",
 CARRIER AGENTS (0356)
 VAGINA
 9,10-DIMETHYL-1,2-BENZANTHRACENE,
 SARCOMA, CARCINOMA (0441)
 VECTOR
 COCKROACH, LYMPHOSARCOMA, TOAD (0615)
 VIRUS
 ADENOVIRUS, CHROMOSOME ABERRATION
 (0686)*
 ADENOVIRUS SA7, TRANSFORMED CELLS
 TRANSPLANTATION ANTIGEN, HAMSTER
 (0616)
 ADENOVIRUS, SV40, INHIBITION OF

SUPERINFECTION (0612)
 ENOVIRUS TYPE 2, STRUCTURAL PRO-
 TEINS, DEGRADATION PRODUCTS (0613)
 ENOVIRUS TYPE 7, ERYTHROCYTES,
 VIRAL ADSORPTION (0614)
 ENOVIRUS TYPE 12, HETEROKARYOCYTES,
 PERMISSIVE AND NONPERMISSIVE CELL
 FUSION (0611)
 ENOVIRUS TYPE 12, SARCOMA,
 IMMUNOLOGY, HAMSTER (0618)
 ENOVIRUS TYPE 12, SPLEEN LYMPHOID
 CELLS, INHIBITION OF TUMOR GROWTH
 (0617)
 TYPE VIRUS-LIKE PARTICLES, MURINE
 PLASMA CELL NEOPLASIA, PARAPROTEIN
 (0593)
 AN MYELOBLASTOSIS, AMINO ACID
 ACCEPTOR RNA, AMINOACYLATION
 CAPACITY (0585)
 AN MYELOBLASTOSIS, DNA POLYMERASE
 ACTIVITY, RNA (0584)
 AN MYELOBLASTOSIS, GROUP-SPECIFIC
 ANTIGEN (0582)
 AN MYELOBLASTOSIS, NUCLEOCAPSID
 STRUCTURE (0587)
 AN MYELOBLASTOSIS, POLYMERASE, RNA,
 DNA (0586)
 AN MYELOBLASTOSIS, TRANSFORMATION,
 HEMATOPOIETIC CELLS (0583)
 AN SARCOMA, UV IRRADIATION, TRANS-
 FORMING CAPACITY (0640)
 AN SARCOMA, VISIBLE LIGHT,
 5-BROMODEOXYURIDINE, CHICK EMBRYO
 FIBROBLAST (0641)
 AN TUMOR, STRAIN MC29, TUMORIGENE-
 SIS, CHICKS (0580)
 FINE SYNCYTIAL, LYMPHOSARCOMATOUS
 CATTLE, MORPHOLOGICAL VIRAL VARIANT
 (0561)
 BURKITT'S LYMPHOMA, IMMUNOSUPPRESSION
 (0687)*
 CANCER VIRUS, NUCLEIC ACIDS-HYBRIDIZA-
 TION (0554)
 CELL-FREE ORGAN EXTRACTS, MURINE
 MYELOID LEUKEMIA, LEUKEMIA INDUCTION
 (0605)
 CELL-FREE THYMIC SUPERNATANTS, GENETIC
 SUSCEPTIBILITY, THYMIC LYMPHOMA
 (0594)
 TYPE RNA, DNA POLYMERASE ACTIVITY
 (0555)
 TYPE SARCOMA, B-TYPE MOUSE MAMMARY
 TUMOR, LEUKEMIA, POLYMERASE (0589)
 TYPE VIRUS PARTICLES, ENVELOPE
 SPIKES, FELINE LYMPHOMA (0588)
 GITAL FIBROUS TUMOR, CYTOPLASMIC
 INCLUSIONS (0795)
 A VIRUS-TRANSFORMED CELL LINES,
 ENZYMIC BLOCK, GANGLIOSIDE SYNTHESIS
 (0568)
 EPSTEIN-BARR, BURKITT'S LYMPHOMA,
 MORPHOLOGY (0575)
 EPSTEIN-BARR, BURKITT'S LYMPHOMA,
 NASOPHARYNGEAL CARCINOMA, DNA (0574)
 EPSTEIN-BARR, C MARKER CHROMOSOME
 (0576)
 EPSTEIN-BARR, HUMAN EMBRYONIC CELL
 LINE, LEUKEMIA (0570)
 EPSTEIN-BARR, INFECTIOUS MONONUCLEOSIS
 (0553), (0577)

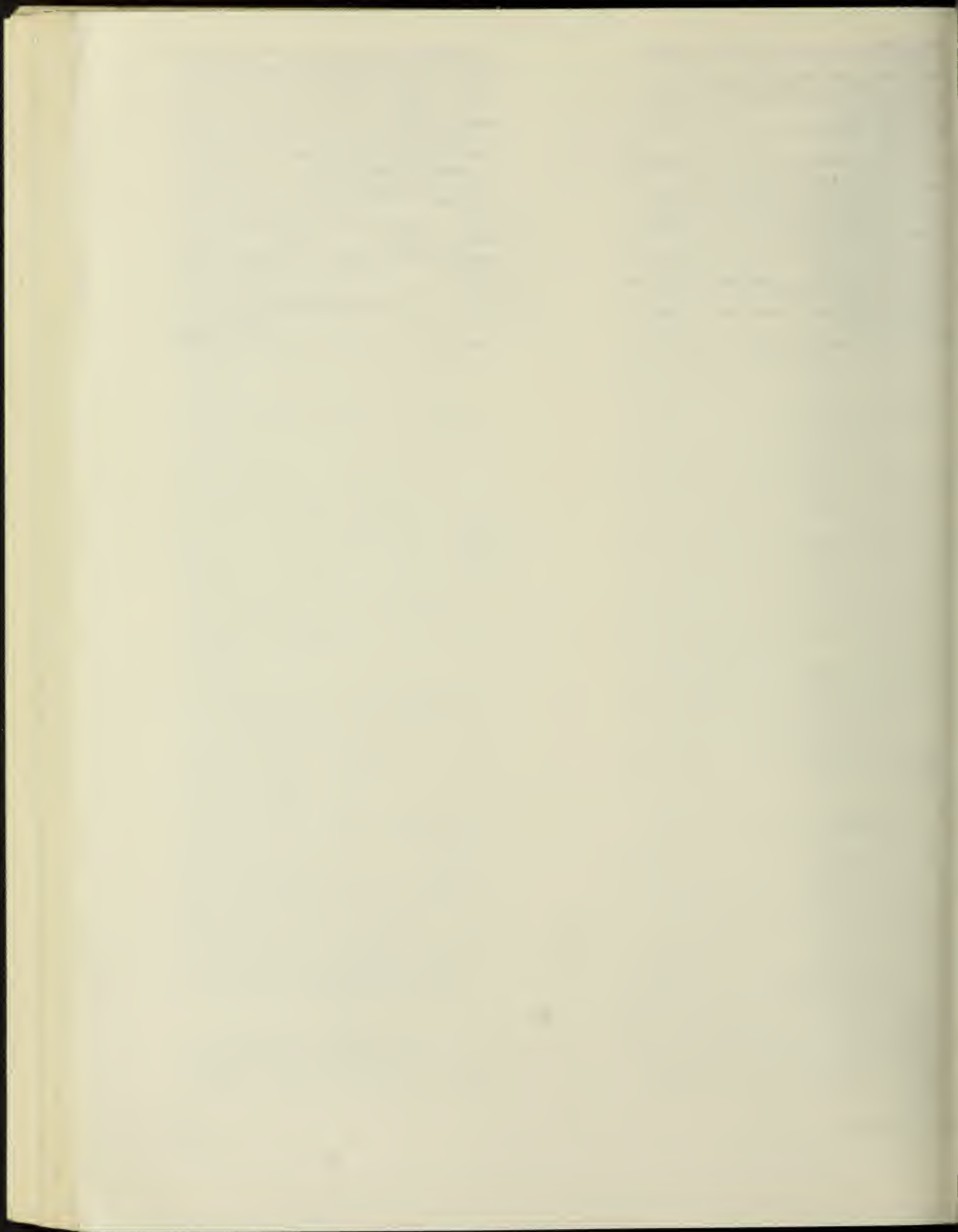
EPSTEIN-BARR, MEMBRANE ANTIGEN,
 BURKITT'S LYMPHOMA, NASOPHARYNGEAL
 CARCINOMA (0578)
 EPSTEIN-BARR, NASOPHARYNGEAL CARCINOMA
 SURFACE ANTIGEN (0579)
 EPSTEIN-BARR, SERUM ANTIBODY TITRATION
 (0571)
 EPSTEIN-BARR, SERUM ANTIBODY TITRATION
 CHILDREN (0758)
 EPSTEIN-BARR, VIRAL DNA, BURKITT'S
 LYMPHOMA (0688)*
 ETIOLOGY, HISTOLOGY, NASAL PAPILLOMA-
 TOSIS (0373)
 FBJ BONE TUMORS (0561)
 FRIEND, NUCLEAR RNA SYNTHESIS (0601)
 FRIEND, POLIOVIRUS, ECHOVIRUS,
 LEUKEMIA, RNA (0572)
 FRIEND LEUKEMIA, CELL COLONY-FORMING
 ABILITY (0603)
 FRIEND LEUKEMIA, GUAROA, ENHANCEMENT
 (0602)
 FROG VIRUS 3, DNA REPLICATION, GAMMA
 RAYS (0522)
 GROSS LEUKEMIA, X-IRRADIATION
 SYNERGISM, LEUKEMOGENESIS (0604)
 HAMSTER-SPECIFIC C-TYPE, GROUP
 SPECIFIC ANTIGEN (0552)
 HAMSTER-SPECIFIC SARCOMA, ENVELOPE
 ANTIGEN RELATIONSHIPS (0551)
 HARVEY MURINE SARCOMA, INTERFERON,
 MORTALITY (0639)
 HEMAGGLUTINATION-INHIBITION, INFEC-
 TIVITY, RAT (0559)
 HERPES SAIMIRI, MORPHOLOGICAL CLASSI-
 FICATION (0619)
 HERPES SIMPLEX, ANTIGENS, CERVICAL
 CARCINOMA (0623)
 HERPES SIMPLEX, CERVICAL EPITHELIUM,
 HUMAN (0620)
 HERPES-TYPE VIRUS, NASOPHARYNGEAL
 CARCINOMA, LYMPHOBLASTOID TRANS-
 FORMATION (0625)
 HERPES VIRUS, ENDOMETRIUM (0622)
 HERPES VIRUS TYPE 2, ANTIBODIES,
 INVASIVE CERVICAL CARCINOMA (0624)
 HUMAN LEUKEMIA, REVERSE TRANSCRIPTASE
 (0352)
 INFLUENZA, LUNG CANCER, MICE, CELL
 METAPLASIA (0564)
 LACTIC DEHYDROGENASE PASSENGER,
 RAUSCHER LEUKEMIA, THYMIC LYMPHOCYTE
 SPLEEN (0609)
 LATENT ONCOGENIC, PRECIPITATING FACTOR
 LEUKEMIA (0351)
 LEUKEMIA, COMPLEMENT BINDING, ANTIGENS
 RABBIT, MAN (0711)
 LEUKEMIA, MOUSE, SPLEEN, WHOLE BODY
 IRRADIATION (0592)
 LEUKOVIRUS, HUMAN, HEMATOPOIETIC
 (0571)
 LUCKE ADENOCARCINOMA FROG HERPESVIRUS,
 BURKITT'S LYMPHOMA, VIRAL DNA
 DENSITIES (0621)
 LYMPHOSARCOMA AND LEUKEMIA VIRUS
 PARTICLES, MORPHOLOGY AND DISTRIBU-
 TION (0550)
 MAMMARY TUMOR, BRAIN AND LIVER
 EXTRACTS, GR STRAIN MICE (0629)
 MAMMARY TUMOR, MAMMARY CARCINOMA
 (0633)

MAMMARY TUMOR, MILK TRANSMISSION IN MICE, GENETIC SUSCEPTIBILITY TRANSMISSION (0631)
 MAREK'S DISEASE, SENDAI (0581)
 MOLONEY, OSTEOSARCOMA, RAT (0637)
 MOLONEY, RAUSCHER, IMMUNITY, MOUSE (0635)
 MOLONEY LEUKEMOGENIC, PLASMODIUM BERGHEI YOELII, LYMPHOMA (0600)
 MOUSE MAMMARY TUMOR, GENETIC TRANSMISSION (0627)
 MURINE C-TYPE RNA, GROUP-SPECIFIC ANTIGEN (0597)
 MURINE LEUKEMIA, ANTIGEN, LOW-LEUKEMIC STRAIN MICE (0596)
 MURINE LEUKEMIA, CROSS IMMUNIZATION, INTERFEROGENESIS (0595)
 MURINE LEUKEMIA, GROUP-SPECIFIC ANTIGEN (0598)
 MURINE LEUKEMIA, RESCUE OF PSEUDOTYPE SARCOMA, NEW ZEALAND BLACK MICE (0606)
 MURINE LEUKEMIA, THYMIC LYMPHOMA, ALKALINE PHOSPHATASE, RAT (0590)
 MURINE SARCOMA, CELL MULTIPLICATION (0636)
 MURINE SARCOMA, DNA POLYMERASE, RNA (0634)
 MURINE SARCOMA, MURINE LEUKEMIA, NONPRODUCER VIRAL CLONES (0638)
 ONCOGENIC, POLYMERASE, NUCLEIC ACID (0553)
 PAPOVA, THYMUS, LIVER, LEUKEMIA (0672)
 PARTICLES, HUMAN LEUKEMIA AND LYMPHOMA (0569)
 PARTICLES, MEDIASTINAL LYMPHOMA, LUNG EPITHELIOMA, URETHAN, GERM-FREE MOUSE (0494)
 PARTICLES, PLASMA CELL GRANULOMA, MINERAL OIL (0396)
 PARTICLES, RAT MAMMARY ADENOCARCINOMA (0630)
 PARTICLES, THYMUS, EPIDIDYMIS, HEMATOPOIETIC ORGANS, MOUSE (0632)
 POLYOMA, AGGLUTININ, CONTACT INHIBITION, CONCAVALIN A (0679)
 POLYOMA, CELL TRANSFORMATION, VIRUS GENERATION IN VITRO (0667)
 POLYOMA, HAMSTER KIDNEY CELL CULTURE, ENDONUCLEASE (0674)
 POLYOMA, HOST RANGE MUTANTS (0681)
 POLYOMA, INHIBITION OF ONCOGENESIS, POLYRIBOINOSINIC-POLYRIBOCYTIDYLIC ACID (0685)
 POLYOMA, MOUSE KIDNEY CELL CULTURE, DNA SYNTHESIS, T-ANTIGEN (0676)
 POLYOMA, NON-TRANSFORMING MUTANT, CELL MEMBRANE AGGLUTINATION (0680)
 POLYOMA, ROUS SARCOMA, SENDAI, EMBRYONIC HUMAN FIBROBLAST (0675)
 POLYOMA, SPLENIC LYMPHOID TUMORS, ANTI-THYMOCYTE SERUM (0682)
 POLYOMA, SV40, ADENOVIRUS, TRANSFORMED-CELL SURFACE MEMBRANE, AGGLUTINATION (0708)
 POLYOMA, SV40, PURIFICATION BY POLYETHYLENE GLYCOL PRECIPITATION (0684)
 POLYOMA, TEMPERATURE-SENSITIVE MUTANT

POLYOMA VIRUS, 3T3 CULTURE, BALB/C-3T3 CULTURE (0673)
 POLYOMA, TEMPERATURE-SENSITIVE POLYOMA MUTANT, INTERFERON, DNA, 3T3 CELL CULTURE (0678)
 POLYOMA, 3T3 MOUSE CELL, BHK21 HAMSTER CELL, GROWTH REGULATION (0350)
 POLYOMA PSEUDOVIRUS, UNCOATING, MOUSE EMBRYO CELLS (0683)
 RAUSCHER, POLYRIBOSOME, SPLEEN, MOUSE (0607)
 RAUSCHER MURINE LEUKEMIA, LEUKEMOGENESIS, AEROSOL EXPOSURE (0608)
 RNA, DNA, REVIEW* (0381)*
 RNA, RNA-DEPENDENT, DNA POLYMERASE, ONCOGENIC (0557)
 RNA TUMOR, GROUP-SPECIFIC ANTIGEN (0562)
 RNA-TYPE, ISOLATION, MONKEY MAMMARY CARCINOMA (0626)
 ROUS, POLYOMA, CELL TRANSFORMATION STAGES, HAMSTER (0556)
 ROUS SARCOMA, ANTIGENS, "VIRUS FREE" TUMORS (0655)
 ROUS SARCOMA, AVIAN LEUKOSIS, CHICK EMBRYO CELL CULTURE, DNA SYNTHESIS (0566)
 ROUS SARCOMA, EMBRYONIC TISSUE CULTURES, GRAFT (0654)
 ROUS SARCOMA, KARYOTYPES OF TUMOR CELL (0591)
 ROUS SARCOMA, LOW MOLECULAR WEIGHT RNA, 4S (0646)
 ROUS SARCOMA, POLYMERASE (0648)
 ROUS SARCOMA, POLYMERASE, ENDONUCLEASE RNA, DNA (0647)
 ROUS SARCOMA, POLYMERASE, RNA, DNA (0651)
 ROUS SARCOMA, POLYOMA, SARCOMA 180, PROLIFERATION (0814)
 ROUS SARCOMA, RABIES VIRUS VACCINE, CHICKEN (0652)
 ROUS SARCOMA, RNA SYNTHESIS, BROMODEOXYURIDINE (0645)
 ROUS SARCOMA, SARCOMA VOLE (0642)
 ROUS SARCOMA, SONIC DISRUPTION, OVERGROWTH STIMULATING ACTIVITY (0644)
 ROUS SARCOMA, TUMOR RECURRENCE (0650)
 ROUS SARCOMA, TUMOR SPECIFIC ANTIGEN, MOUSE (0653)
 ROUS SARCOMA, URIDINE METABOLISM, CHICK CHORIOALLANTOIC MEMBRANE (0643)
 ROUS SARCOMA, VESICULAR STOMATITIS, SMALLPOX VACCINE (0560)
 ROUS SARCOMA MUTANT, FUSIFORM CELL TRANSFORMATION (0649)
 ROWSON-PARR, INDUCTION OF LYMPHOMA, MICE (0610)
 SCHMIDT-RUPPIN ROUS, SARCOMA, THYMUS, CHICKEN (0656)
 SHOPE FIBROMA, FOCUS FORMATION, NUCLEIC ACID SYNTHESIS (0657)
 SHOPE PAPILLOMA, ANTIGENICITY (0658)
 SV40, ADENOVIRUS HYBRID, TRANSFORMATION, ANTIGEN (0615)
 SV40, ADENOVIRUS TYPE 12, ORNITHINE, LEUCINE POLYMER, AGGREGATION OF TRANSFORMED CELLS (0661)

SV40, ANTI-MOUSE EGG ANTIGEN, CYTO-
TOXICITY (0669)
SV40, CELL TRANSFORMATION, TUMOR-
ANTIGEN PRODUCTION (0349)
SV40, DNA, TRANSFORMATION SUSCEPTI-
BILITY (0659)
SV40, DNA SYNTHESIS, ACTINOMYCIN D
(0662)
SV40, ENHANCEMENT OF VIRAL TRANSFORMA-
TION, UV IRRADIATION (0663)
SV40, IMMUNIZATION DURING LATENCY,
TUMORIGENESIS INHIBITION (0671)
SV40, INDUCTION, MITOMYCIN C, OTHER
AGENTS (0660)
SV40, KIDNEY CELL, THYMIDINE KINASE,
HAMSTER (0667)
SV40, MITOMYCIN C, 5-BROMODEOXYRUIDINE
MOUSE KIDNEY CELLS (0664)
SV40, MYCOPLASMA, CHROMOSOME ABERRA-
TIONS (0665)
SV40, POLYOMA, CHROMOSOME MODALITY,

REVERSION, MOUSE CELL LINE (0558)
SV40, TEMPERATURE-SENSITIVE REPLICA-
TION, MUTANT (0666)
SV40, TRANSPLANTATION ANTIGEN INDUC-
TION (0670)
SV40, UV IRRADIATION, SURVIVAL (0668)
TRANSFORMATION, REVIEW (0390)*
TUMOR INDUCTION, CELL-FREE EXTRACT,
NEUROBLASTOMA (0567)
VIRAL ETIOLOGY, LEUKEMIA IN DOMESTIC
ANIMALS, REVIEW (0389)*
VITILIGO
ANEMIA, GASTRIC CARCINOMA (0777)
WALKER'S CARCINOMA
GASTRIC WALL, GROWTH, METASTASES, RAT
(0763)
YTTERBIUM
GADOLINIUM, CARCINOGENESIS (0403)
ZINC
SKIN NEOPLASIA, LEUKOCYTE ZINC CONTENT
(0787)





U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

OFFICIAL BUSINESS

PENALTY FOR PRIVATE USE, \$300

If you do not desire to continue receiving this publication, please CHECK HERE ☐;
tear off this label and return it to the above address. Your name will then be
promptly removed from the appropriate mailing list.

15
Vet
Med.

NOVEMBER-DECEMBER 1970

Abstract Nos. 831-1266

**Vol. 9
No. 5-6**

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health



CARCINOGENESIS ABSTRACTS

A monthly publication of the

National Cancer Institute

Editor

Robert Love, M.D.
Jefferson Medical College, Philadelphia

Associate Editor

George P. Studzinski, M.D.
Jefferson Medical College, Philadelphia

NCI Staff Consultants

Howard R. Rosenberg, M.S.
Sidney Siegel, Ph.D.
Elizabeth Weisberger, Ph.D.

Literature Selected, Abstracted, and Indexed
by

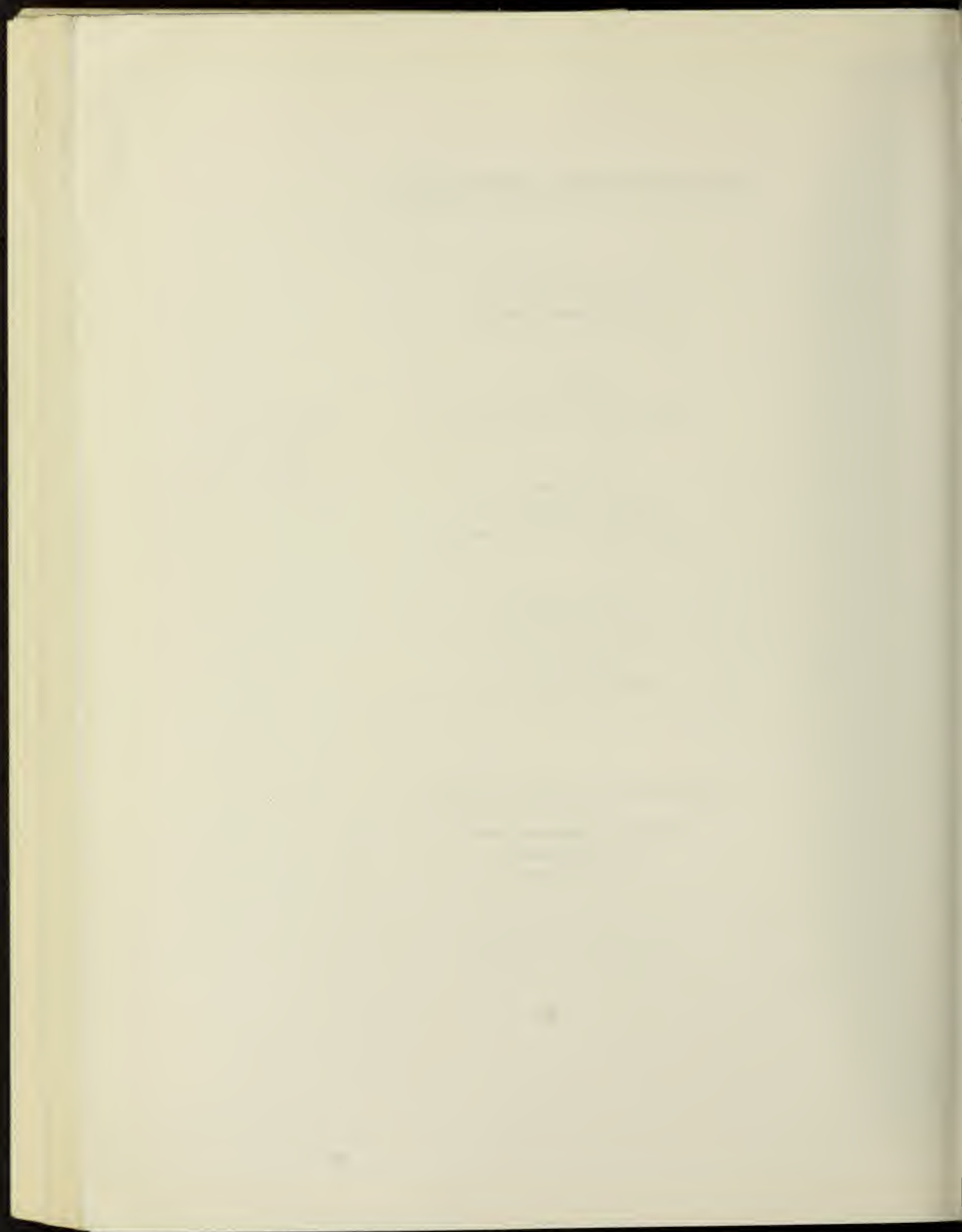
The Franklin Institute Research Laboratories
Science Information Services
Biomedical Section

M. H. Fukami, Ph.D., Technical Editor

Contract Number NIH-71-2073

Public Health Service, USDHEW

THE LIBRARY OF THE
AUG 11 1971
UNIVERSITY OF ILLINOIS
AT CHICAGO



PREFACE

Carcinogenesis Abstracts is a publication of the National Cancer Institute. The journal serves as a vehicle through which current documentation of carcinogenesis research highlights are compiled, condensed, and disseminated on a regular basis. It represents an integral part of the Institute's program of fostering and supporting coordinated research into cancer etiology. Issues of *Carcinogenesis Abstracts* normally contain two-hundred abstracts and twenty citations (unaccompanied by corresponding abstracts). Abstracts and citations refer to the current scientific literature that describes the most significant carcinogenesis research carried on at the National Cancer Institute, other governmental agencies, and private institutions. *Carcinogenesis Abstracts* is intended to be a highly useful current awareness tool for scientists engaged in carcinogenesis research or related areas. The great number and diversity of publications relevant to carcinogenesis make imperative the availability of this service to investigators whose work requires that they keep abreast with current developments in the field.

Carcinogenesis Abstracts is normally published monthly. Volume IX covers the scientific literature published from July 1970 through June 1971. A cumulative subject and author index for Volume IX will be published shortly after the final regular issue. This journal is available free of charge to libraries and to individuals who have a professional interest in carcinogenesis. Requests for *Carcinogenesis Abstracts* from qualified individuals should include statements of their relationship to carcinogenesis research. All correspondence should be addressed as follows:

Carcinogenesis Abstracts
Etiology Area
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20014

Use of funds for printing this publication
approved by the Director of the Bureau of
the Budget on July 25, 1967.



NOTE

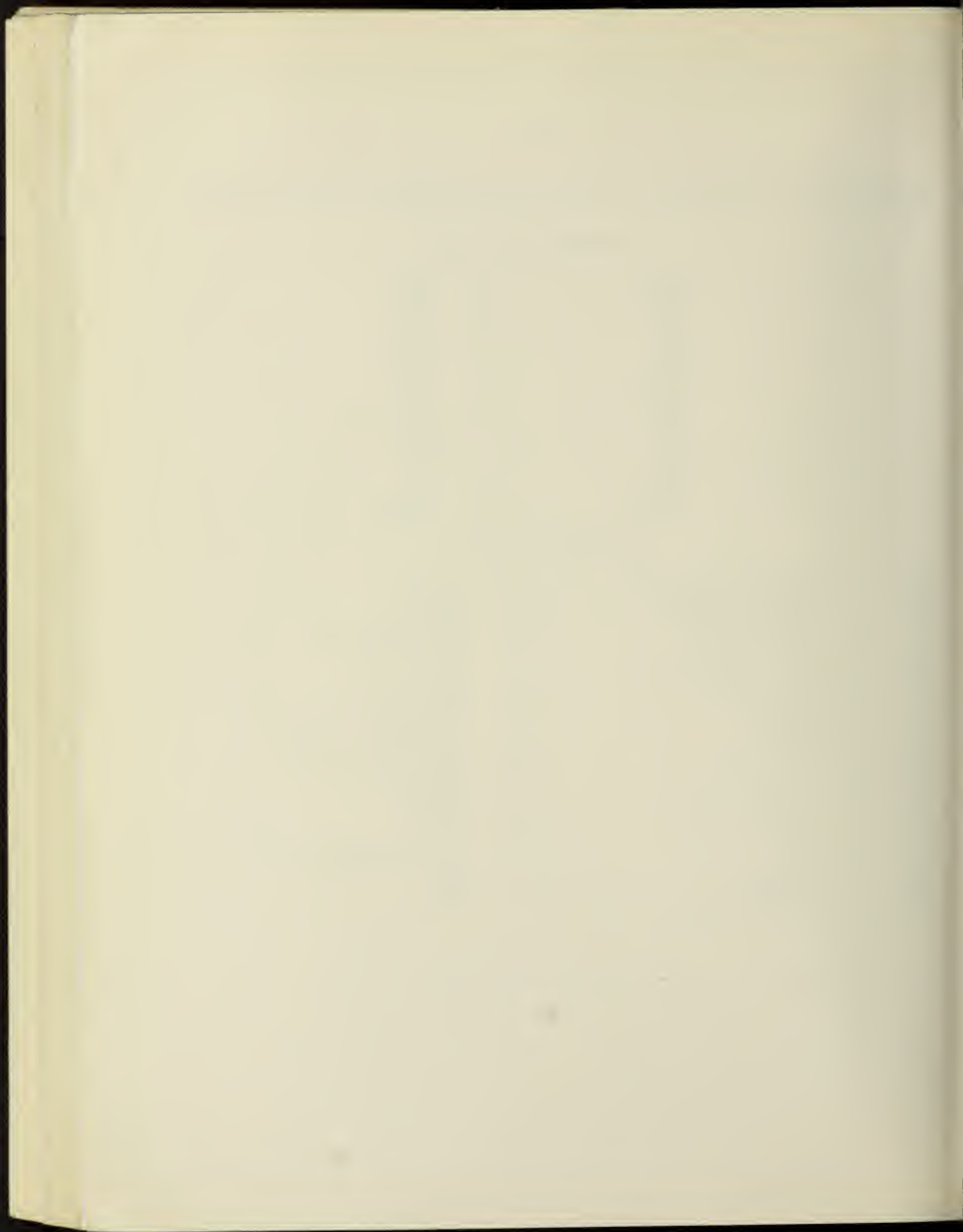
Journal names are abbreviated according to the list of abbreviations used by *Index Medicus*. For journals not covered by *Index Medicus*, the abbreviations (with some modifications) found in *World Medical Periodicals*, 3rd Edition, are used.

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	It.	Italian
Ar.	Arabic	Jap.	Japanese
Bul.	Bulgarian	Kor.	Korean
Ch.	Chinese	Latv.	Latvian
Cz.	Czech	Lith.	Lithuanian
Dan.	Danish	Nor.	Norwegian
Dut.	Dutch	Pol.	Polish
E.	English	Por.	Portuguese
Eston.	Estonian	Rum.	Rumanian
Fin.	Finnish	Rus.	Russian
Fl.	Flemish	Ser.	Serbo-Croatian
Fr.	French	Sl.	Slovak
Ger.	German	Sp.	Spanish
Gr.	Greek	Sw.	Swedish
Heb.	Hebrew	Th.	Thai
Hun.	Hungarian	Turk.	Turkish
Ic.	Icelandic	Uk.	Ukrainian
ln.	Indonesian	Viet.	Vietnamese

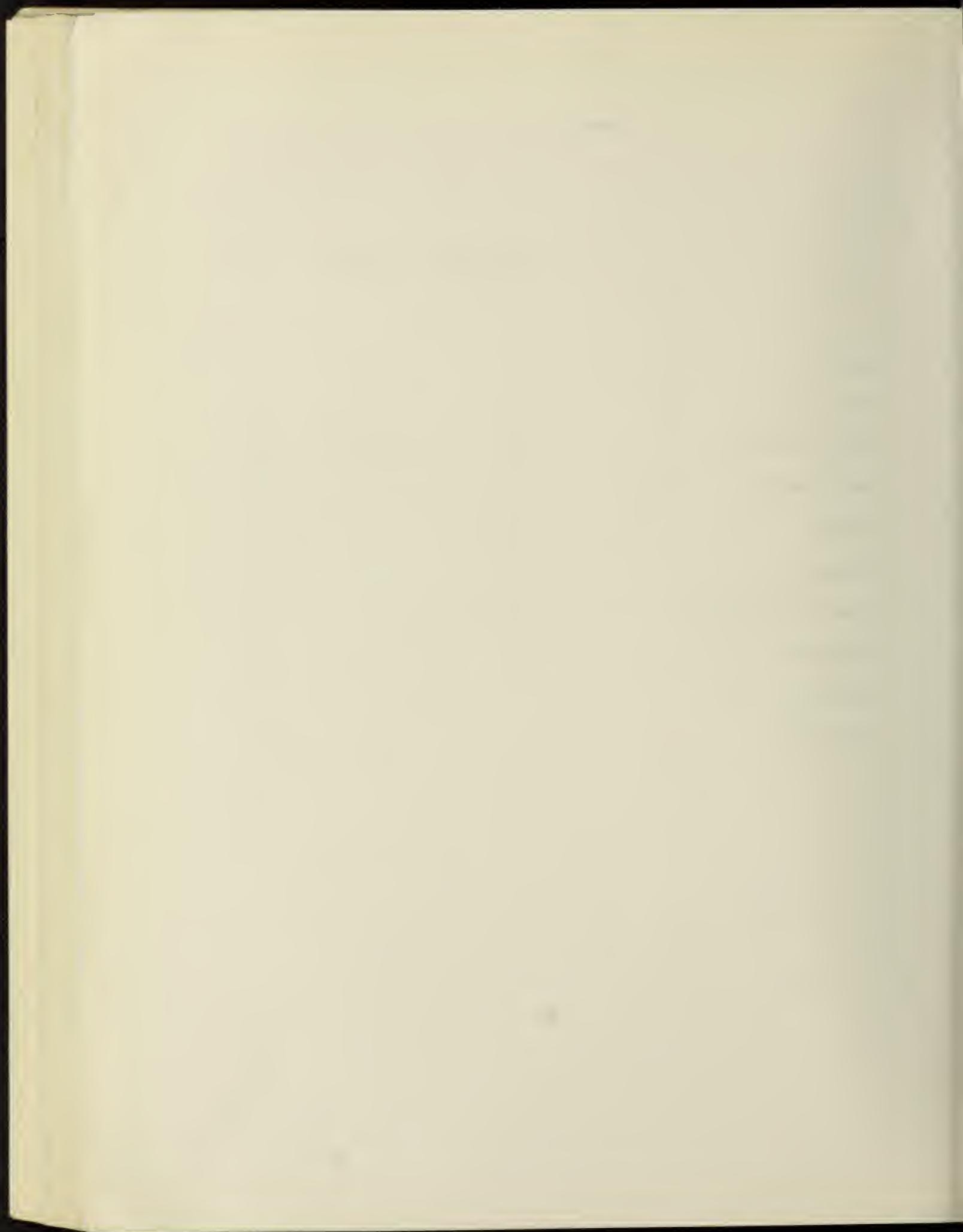
ABBREVIATIONS USED IN ABSTRACTS

ACTH	adrenocorticotrophic hormone	mg	milligram(s)
ADP	adenosine diphosphate	min	minute(s)
AMP	adenosine monophosphate	ml	milliliter(s)
ATP	adenosine triphosphate	mm	millimeter(s)
C	degrees centigrade	MTD	maximum tolerated dose
cm	centimeter(s)	ng	nanogram (10^{-9})
CNS	central nervous system	pg	picogram (10^{-12})
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	ppm	parts per million
e.g.	for example	r	Roentgen
g	gram(s)	RBC	red blood cells (erythrocytes), red blood count
µg	microgram(s)	resp.	respectively
hr	hour(s)	Rev.	review (only in citations)
i.m.	intramuscular	RNA	ribonucleic acid
i.p.	intraperitoneal	s.c.	subcutaneous
IU	international unit(s)	sec	second(s)
i.v.	intravenous	U	unit(s)
kg	kilogram(s)	UV	ultraviolet
LD ₅₀	median lethal dose(s)	WBC	white blood cells (leukocytes), white blood count
m	meter(s)	wk	week
M	molar	wt	weight
mEq	milliequivalent(s)	yr	year(s)
mM	millimolar		
µM	micromolar		
mC, µC	milli-,microcurie(s)		



CONTENTS

	Cross Reference Abbreviations	Abstracts, Citations	Page
REVIEW	(Rev).	0831-0883	173
CHEMICAL CARCINOGENESIS.	(Chem)	0884-0991	183
PHYSICAL CARCINOGENESIS.	(Phys)	0992-1016	210
VIRAL CARCINOGENESIS	(Viral).	1017-1115	217
IMMUNOLOGY	(Immun).	1116-1142	242
PATHOGENESIS	(Path)	1143-1164	249
EPIDEMIOLOGY AND BIOMETRY.	(Epid-Biom).	1165-1195	254
MISCELLANEOUS.	(Misc)	1196-1276	261
AUTHOR INDEX			i
SUBJECT INDEX.			xi



- 831 TRANSFER RNA METHYLASES AND CANCER. (E.) Craddock, V. M. (MRC Lab., Carshalton, Surrey, England). *Nature* 228(5278):1264-1268, 1970.

The experimental basis and the possible significance of changes in activities of nucleic acid methylases in tumors are reviewed. The tRNA methylases alkylate each of the 4 major bases and also the 2' position of the ribose moiety. In normal conditions, tRNA of a given species as isolated is fully methylated *in vivo*, but because the methylases are species specific, the incubation of tRNA from one species with methylases from another species can lead to further methylation; for this reason, activities of methylases in tumors have been studied by use of other than normal substrates. Changes in methylase activities in tumors may involve a change of specificities so that different proportions of bases are methylated, or there may have been an alteration in tRNA transcription, which could result in an altered substrate for the methylases. Measurement of methylated bases in urine from patients with leukemia often show an increased excretion of 7-methylguanine or 8-hydroxy-7-methylguanine, but this is not general among cancer patients with solid tumors. Studies with ¹⁴C-labeled bases and analysis of isolated tRNA in laboratory animals have confirmed that methylation is often altered in malignancy and high excretion of methylated bases in cancer patients is probably not an artifact due to increased cell death and degradation. The carcinogenic event associated with ethionine might be due to methylation of bases by way of S-adenosylethionine. The biochemical consequences of altered methylation may be due to alterations in binding interactions or codon recognition, which may result in variation of synthesis of some protein regulator of differentiation and other protein synthesis. (55 references)

- 832 MALADIES OF DEREPRESSION: PATHOLOGICAL, OFTEN MONOCLONAL, DEREPRESSION OF PROTEIN FORMING TEMPLATES. (E.) Waldenström, J. (Allmänna Hosp., Malmö, Sweden). *Schweiz Med Wschr* 100(51):197-2206, 1970.

The production of proteins by neoplastic and paraneoplastic cell systems from various sites are reviewed. Hypercalcemia is among the paraneoplastic phenomena observed in patients with malignant disease. A number of similar paraneoplastic symptoms may be explained as ectopic formation of polypeptide hormones. Since templates for the synthesis of polypeptides are present in a dormant, repressed state in the genome of all cells, it seems possible that ectopic polypeptide formation in neoplastic and paraneoplastic systems is a phenomenon of derepression of fetal protein synthesis. Support for this hypothesis comes from the finding that a fetal protein, fetuin, is produced by malignant hepatoma cells. Fetal Hgb globulin has been detected in large amounts in a patient with thalassemia; placental isoenzyme of alkaline phosphatase has been found in sera from 27 patients with lung, liver, and ovary tumors. Water intoxication, which appears as a paraneoplastic concomitant in some carcinoma cases, has been found to be due to ectopic formation of an antidiuretic hormone. The pituitary

hormone ACTH and melanophore stimulating hormone are produced by various carcinomas. Other hormones produced ectopically by tumors, perhaps as a result of derepressed fetal polypeptide systems, include calcitonin, amyloid, erythropoietin, Bence-Jones protein, cold agglutinin, and monoclonal cryoglobulins. It has recently been shown that tumors arising from immunocytes produce monoclonal proteins; it may be that in such clones of cells only 1 protein template is activated. Many of the instances of ectopic protein synthesis listed above appear to represent a monoclonal derepression of fetal protein forming templates. (51 references)

- 0833 CARCINOGEN BINDING BY CELL PROTEINS AND THE "DROP OUT" HYPOTHESIS. (Rus.) Bannikov, G. A. (Inst. Experim. and Clin. Oncol. Acad. Med. Sci. USSR). *Vop Onkol* 16(9):115-121, 1970.

The role of carcinogen binding by cell proteins which is associated with the disappearance of specific regulatory proteins and which produces energetic shifts leading to oncogenesis is reviewed. The target organ specificity of such compounds is illustrated by hepatocarcinogens such as 4-dimethylaminoazobenzene (DAB), fluorenylacetylamide (FAA) and others. DAB is bound by a narrow group of soluble liver proteins referred to as the *h*-fraction, which is characterized by a particularly high methionine content (15 residues/mole) in its amino acid composition; this fraction has been proven to be the binding site of the azodye, and the evidence suggests that covalent linkage is involved. The kinetics of the carcinogen-protein binding show that the accumulation of DAB in rats maintained on a DAB containing diet is linear during the first 3-5 wk and reaches a peak, coinciding with the occurrence of greatest histological alterations in the liver tissue and with the highest mortality rate; the accumulation then decreases to zero at the appearance of the tumor. A decrease in *h*-protein seems to occur along with the decrease in carcinogen binding rate after the peak stage; this decrease in *h*-protein appears to be correlated with the degree of deviation of the preneoplastic tissue from normal liver tissue. A correlation between carcinogenicity and the rate of accumulation of carcinogen in the susceptible tissue has been found for various carcinogens. Two common features associated with the action of various chemical carcinogens are: 1) the formation of a covalent link between the carcinogen and a certain group of soluble proteins of the susceptible tissue and 2) the disappearance, referred to as the "drop out", of these proteins from within the carcinogen-induced neoplastic tissue. (66 references)

- 0834 ESTROGEN-BINDING AND THE HORMONE RESPONSIVENESS OF TUMORS. (E.) King, R. J. B. (Imp. Cancer Res. Fund, London, England), J. A. Smith and A. W. Steggles. *Steroidologia* 1(2):73-88, 1970.

The relation between hormone responsive and unresponsive tumors and estrogen binding is reviewed. Experimental systems used for hormone responsive studies include dimethylbenzanthracene-induced mammary adenocarcinomas, estrogen-induced kidney and pituitary

tumors, the BR6 pregnancy dependent tumor and androgen dependent mammary tumors. In the rat mammary tumor, over 80% of the label after one injection of 6,7-³H-estradiol was found in the nuclear fraction and appeared to be attached to a non-histone protein. Cytoplasmic estradiol seemed to be associated with a high molecular wt protein. Mammary tumors from patients who do not respond to adrenalectomy appear to bind less estrogen than tumors which do respond to the operation. In general, unresponsive tumors appear to be biochemically more active than responsive ones. (54 references)

- 0835 SUNLIGHT AND THE AETIOLOGY OF MALIGNANT MELANOMA: A SYNTHESIS. (E.) Lee, J. A. H. (Sch. Publ. Hlth. Commun. Med., U. Washington, Seattle) and J. M. Merrill. *Med J Aust* 57(18):846-851, 1970.

Data on the anatomical distribution and pathological type of malignant melanoma was collected, and the correlation of these factors with exposure to sunlight was examined. Lentigo maligna, a skin condition which degenerates into invasive malignant melanoma in approximately 33% of cases, is primarily a feature of skin which has been exposed to sunlight for long periods. Incidence rates for New Zealand show that 100 cases of lentigo maligna occurred/million population/yr for persons 55-yr-old, as compared with England and Wales where the incidence rate for 55-yr-olds was 15 cases/million/yr. Superficial spreading melanoma, which makes up most cases of melanoma of the female lower limbs, has excessive incidence on areas of the leg exposed to sunlight. Although there is evidence that the incidence of malignant melanoma itself is related to the degree of exposure of populations to sunlight, attempts to relate distribution of malignant melanoma to exposed sites by taking histories from individuals have not been fruitful. No evidence has been found that specifically exposed areas of the body, such as the head and neck, have unusually high incidences of malignant melanomas. However, malignant melanoma of all sites has a higher incidence in equatorial countries (e.g., 164 cases/million population/yr in New Zealand) than in northern countries (e.g., 18 cases/million/yr in Denmark). Nodular melanoma, tumors which are uniformly invasive and which involve the worst prognosis of the melanoma conditions, are not particularly associated with sunlight exposure. It has been suggested that, since exposed areas of the body are not necessarily the site of increases in incidence of malignant melanoma, sunlight may exert an indirect effect on malignant melanoma pathogenesis. A systemic effect associated with latitude might involve heat, perspiration or minor trauma associated with rubbing clothing. A circulating factor which is sensitive to sunlight may be operative in the increased incidence of malignant melanoma (e.g., chalones, which control the rate of mitoses in the skin and which be modified by exposure to sunlight. (41 references)

- 0836 THE MALIGNANT TUMOR RISK FROM RADIUM BODY BURDENS. (E.) Goss, S. G. (Radiol. Protect. Service, Belmont, Sutton, Surrey, England). *Health Phys* 19(6):731-737, 1970.

Studies on malignancy risk as a result of exposure to radium in supposedly "acceptable" doses conducted by 2 groups (MIT and ANL) are discussed. These studies have asserted that large safety factors operate for the presently-accepted maximum permissible dose of 0.1 μ C of ²²⁶Ra; it was implied that there are practical thresholds of the body burden of radium at higher levels. However, these studies were conducted on small sample populations of radium-exposed persons, only half the populations at risk were located and studied, and the conclusions were based on oversimplified assumptions on the mechanism of tumorigenesis by radium, which is, in fact, obscure. The studies conclude that for the induction of tumors by radium, a threshold level exists above that given by the present maximum permissible level for ²²⁶Ra in the body; however, insufficient attention was paid to the fact that the possibility of tumor incidence at low radium doses is small enough for no tumors to have appeared in the few exposed persons examined. The threshold levels arrived at by the studies might still be unacceptable if exposed to larger populations. Since a high proportion of the populations studied are still alive, many of the histories from these populations are incomplete; the higher than expected tumor incidence manifested in 1 study suggests that the range of radium-induced tumors may be wider than expected. Dose-response curves for radium were calculated in the absence of theory to indicate which dose parameter is appropriate for defining the curve. It is concluded that no factor of safety or high threshold of radium body burden has been shown to exist, and that the present maximum permissible level for ²²⁶Ra in the body is, if anything, too high. (15 references)

- 0837 COMMON PROPERTIES OF THE ONCOGENIC RNA VIRUSES (ONCORNAVIRUSES). (E.) Nowinski, R. C. (Sloan-Kettering Inst. Cancer Res., New York, N.Y.), L. J. Old, N. H. Sarkar and D. H. Moore. *Virology* 42(4):1152-1157, 1970.

The biological, biochemical, and structural properties of the oncornaviruses, or oncogenic RNA viruses, are reviewed. Biologically, all oncornaviruses are oncogenic to some degree in their natural hosts, which include most vertebrates in which thorough investigations for the presence of the viruses have been made. Oncornaviruses commonly induce leukemias, sarcomas and mammary tumors. Congenital infection by oncornavirus is more frequent than postnatal infection; some oncornavirus characteristics show Mendelian inheritance. Oncornaviruses do not produce a cytopathic effect in the infected cells of their hosts. Oncornaviruses have a 60-70S RNA, and a small basic protein as the prominent group-specific antigen; they rarely show hemagglutinating activity *in vivo*. Actinomycin treatment usually inhibits the production of oncornaviruses by chronically infected cells *in vitro*. Oncornaviruses contain an enzyme which produces DNA from a viral RNA template. Structurally, the oncornaviruses display a spherical internal structure, as opposed to a cubic or helical symmetry. The nucleoprotein of the oncornaviruses is apparently a 30 A strand which is free in disrupted particles and takes a helical form in intact viruses. (47 references)

0838 SOMATIC HYBRIDIZATION AND CELL MALIGNANCY. (Fr.) Barski, G. (Inst. Gustave Roussy, Villejuif, France). *Bull Cancer* 57(2):185-194, 1970.

Experimental data on malignant and nonmalignant cell hybridization accumulated since 1960 are reviewed and the complexity of factors determining the properties of daughter cells is discussed. When N2 cells (clone NCTC 2 555) without tumorigenic properties and N1 cells (clone NCTC 2 472) with tumorigenic properties are fused and injected into test animals, sarcomas are produced. The hybridization of the N1 and N2 cells produced M cells which in *in vitro* experiments showed a tendency to malignancy, and when injected into the syngeneic mice, the nonmalignant N2 disappeared, and the tumors formed were composed of the hybrid M cell. These were characterized by a cellular morphology intermediate between that of N1 and N2, a cumulative karyotype of N1 and N2 with a tendency to chromosome deletion, and a high tumorigenic capacity similar to that of N1. However, the hereditary mechanisms of cancerization could not be compared to the Mendelian rules; there are no unique recessive or dominant features. A merging of several modifications such as the loss of certain control mechanisms and the acquisition of new properties in cells subjected to transformation by oncogenic viruses seems to occur. (20 references)

0839 MALIGNANT TUMORS IN ORGAN TRANSPLANT RECIPIENTS. (E.) Penn, I. (U. Colorado Med. Ctr., Denver). *Recent Results Cancer Res* 35:1-51, 1970.

Experimental work to date concerning the connection of malignancy and immunologic insufficiency in animals and man was reviewed, with emphasis on malignancy development in organ homograft recipients. Data were compiled on cases in which tumors were present before or at the time of organ transplantation, as well as on cases in which tumors were transmitted with the transplanted organs. The possibility of tumors arising *de novo* subsequent to kidney transplantation was discussed. Evidently reduced immunocompetence occurring spontaneously or produced iatrogenically are associated with increased incidence of malignancy, a finding which accentuates the danger of treating cancer by transplantation of affected organs. In view of the importance of accurate statistical data on malignancy associated with organ transplantation, an informal registry of such malignancies has been established in Denver. (186 references)

0840 EVIDENCE FOR HUMAN CANCER IMMUNITY: A REVIEW. (E.) Piessens, W. F. (Massachusetts Gen. Hosp., Boston). *Cancer* 26(6):1212-1220, 1970.

Evidence for tumor specific antigens (TSA) operating in humans was reviewed. Spontaneous regression of lesions, disappearance of distant metastases after excision of the primary tumor mass, relapse after years of "cure", and large numbers of tumor cells

present in the blood during surgery without development of metastases suggested that TSA exists in human systems. Further evidence may be provided by the association of immunosuppressive therapy and tumor development in human subjects. Homografted tumors in human patients rarely grow successfully; it has been suggested that when they do, their growth is explained by immunotolerance or immunosuppression. Circulating tumor-directed antibodies have been demonstrated in humans with Burkitt's lymphoma and malignant melanoma; the antigenicity of neuroblastoma in humans has also been demonstrated. Tumor-specific, cell-mediated immunity elicited by antigens on the membranes of tumor cells have been detected in malignant melanoma, acute leukemia, and breast tumors. (125 references)

0841 IMMUNOLOGICAL ASPECTS OF CANCER: I. IMMUNOLOGICAL FACTORS AFFECTING TUMOUR GROWTH. (E.) Klein, G. (Karolinska Inst., Stockholm, Sweden). *Brit Med J* 4(5732):418, 1970.

Studies of the antigenic properties of human tumors were briefly reviewed. Immune responses by the host against tumor-associated antigens have been demonstrated in Burkitt's lymphoma, nasopharyngeal carcinoma, osteogenic sarcoma, malignant melanoma, neuroblastoma and carcinoma of the colon and bladder. Cell mediated immunity usually plays the major part in the immune response; humoral antibodies are either ineffective or block the rejection reaction. The antigens responsible for the immune response probably are located on the outside of the cell membrane. Tumor cells in a human host might escape rejection by immune mechanisms by changing or losing their antigenic makeup, as may occur in tumors induced by RNA viruses. Alternatively, tumor cells may survive due to an immunosuppressed state in the host brought about by thymectomy, irradiation, or treatment with antilymphocyte serum. Insufficient release of antigen before the tumor has reached an irreversible stage of development might also account for the survival of tumor cells in a human host. (no references)

0842 THE IMMUNOLOGICAL FUNCTION OF THE THYMUS IN THE DEVELOPMENT OF NEOPLASIAS. (Fr.) Potop, I. (Acad. Med. Sci. Rumania, Bucharest). *Rev Roum Endocr* 7(4):305-314, 1970.

A review of the role of the thymus in carcinogenesis is presented. The thymus intervenes in immunological phenomena by means of the lymphoid cells, and thus dictates the immunological response of the embryo and neonate. These thymic lymphocytes may originate either from a migrating colony, or from a metaplasia. The influence of the thymus upon the number of circulating lymphocytes may be due to lymphocytes leaving the thymus, a hormone secreted by the thymus which stimulates proliferation of lymphocytes in the lymph glands and in the spleen, or by interaction with the growth hormones. A thymectomy effected 24 hr after birth decreases the immunological response in the mouse and rat to cutaneous tumors and foreign grafts. In the adult animal thymectomy decreases the immunological response

to irradiation; sensitivity to radioactivity is more pronounced in the young animal (15-45 days old). From experiments investigating the production of antibodies, it was concluded that the thymus intervenes in immunological functions by interaction with hypophyseal hormones. A thymic graft can reestablish the immunological activity of irradiated or irradiated and thymectomized animals. The administration of calf thymus increases the number of lymphocytes in thymectomized animals, prevents the appearance of the wasting syndrome and protects the animals against viral infection. Nevertheless, in the case of certain viruses (Gross and Moloney), thymectomy produces contrary effects. The production of tumors by carcinogenic agents in thymectomized animals is discussed, and immunoprophylactic measures are envisioned. (112 references)

0843 IMMUNOLOGY OF TUMORS. (E.) Surjan, M. (Natl. Inst. Publ. Hlth., Budapest, Hungary). *Ther Hung* 18(2):55-62, 1970.

Malignant transformation of cells is usually accompanied by the acquisition of tumor-specific antigens which elicit an immune response from the host. Such tumor-specific antigens have been demonstrated for all virus-induced tumors, and for most chemically induced tumors. The strongest antigenicity in tumors induced by chemical carcinogens is found in tumors induced by cyclic hydrocarbons and by methylcholanthrene, and the weakest antigenicity is found in tumors induced by cellophane or multipore membrane. Urethan-induced adenomas have no antigenicity at all. As a rule, the stronger the antigenicity of the chemically induced tumor, the earlier the tumor appears. Among virally induced tumors, those induced by RNA and DNA viruses produce tumor-specific antigens. Active antiviral immunity has been shown to protect against tumors induced by the same virus. Spontaneous tumors are usually of weak antigenicity. While cell-mediated immunity is effective against many antigenic tumors, humoral immune responses vary with different tumor types. In some cases humoral antibodies may enhance tumor growth rather than inhibit it. Congenital or acquired immune deficiency, decline of antibody production with age, and iatrogenic immunosuppression may lead to the promotion of tumor growth. Sera from human subjects with Burkitt's lymphoma have been shown to possess tumor antibodies. Immunotherapy may prove to be a useful tool in the management of malignant disease in humans. (52 references)

0844 HORMONAL DEPENDENCE OF BRAIN TUMORS. (Rus.) Babchin, I. S. (Leningrad, USSR). *Vop Onkol* 16(10):29-31, 1970.

The disruption of hormonal balance and steroid equilibrium may induce mutagenic effects in the brain cell and lead to neoplastic growth. Several examples of such neoplasia are reviewed. Neurinoma of the VIII nerve, with an incidence in females 2 times as high as in males, develops usually at the age of 25-35 yr in association with pregnancy, delivery or nursing. Pinealoma occurs in males 5 times more often than in females; cerebellar medul-

loblastoma occurs twice as often in boys as in girls during the early prepuberal age. The role of hormones in inborn heterotopic brain tumors with a teratoid, dermoid or epidermoid character is still uncertain; these tumors become clinically detectable only at the age of puberty. The considerable importance of hormonal factors (either evident or disguised) in the polyetiological genesis of brain tumors is emphasized. (18 references)

0845 PATHOLOGICAL ALTERATIONS OCCURRING IN ORGANS AND TISSUES FOLLOWING CONTRAST MEDIA AND RADIOACTIVE ISOTOPE APPLICATION. (Ger.) Oehlert W. (no affil). *Langenbecks Arch Chir* 327:229-237, 1970.

Tissue alterations induced by radioactive contrast media are reviewed. Accumulation of thorotrast leads to a damage of the reticuloendothelial system with subsequent cell proliferation, and of the surrounding storage cells where α -particles may migrate and induce specific cell and nuclear alterations. Similar effects are produced by cold and hot lymphography (lipiodol). The oily contrast medium leads to reactions against foreign bodies while ^{131}I causes radiation damage to the surrounding tissue. Occasionally formation of giant endothelial cells within the connective tissue occurs, and leads to a total devastation of the lymph nodes. The cold or "hot" contrast media (lipiodol) may enter the lung in some cases by the thoracic duct, and the lipid accumulates within the lining alveolar cells. The ^{131}I -lipiodol-induced alterations in the lung usually consist of 2 stages as in the case of thorotrast. The accumulation of lipid within the alveolar cells leads to the formation of polynuclear giant cells and proliferation of the connective tissue; the β -particles and γ -radiation from ^{131}I induce an increasing radiation fibrosis of the lung parenchyma. (5 references)

0846 CHANGES IN THE CURRENT CONCEPT OF MALIGNANT MELANOMA. (E.) Mishima, Y. (Wakayama Med. U., Japan). *Curr Probl Derm* 3:51-81, 1970.

Some of the clinical and biological distinctions of nevocytic and melanocytic neoplastic processes are reviewed. "Melanocytoma" includes all tumors derived from junctional or dermal melanocytes and excludes pigment tumors made up of nevus cells. The precancerous stage of epidermal melanocytoma usually develops from lentigo senilis or the melanotic freckle of Hutchinson and lentigo maligna; the criteria of malignant transformation into malignant melanocytoma is based on whether the proliferation of anaplastic melanocytes is limited within the epidermal structure or has invaded the dermis beyond the line of the basement membrane. "Dermal melanocytoma" or the cellular blue nevus refers to pigment cell tumors that develop from melanocytes which have not reached their permanent location in the basal layer. The term malignant nevocytoma refers to the malignant melanoma arising from nevus cells of generally junctional type. Its clinical appearance is a rapidly growing, anaplastic tumor which may or may not show melanin hyperpigmentation. The melanosomes of malignant nevocytoma appear to be cigar-shaped

odies 650-950 μ m x 300-400 μ m and are different from melanosomes of malignant melanocytoma. The malignant melanoma cells often show autophagic activity in areas of focal degradation and necrosis and occur more extensively in malignant nevocytoma than in melanocytoma. (36 references)

0847 CARCINOMA OF THE TONGUE. (E.) Westbury, G. (Westminster Hosp., London, England). *Brit J Hosp Med* 4(5):673-678, 1970.

The incidence, etiology and pathology of carcinoma of the tongue were investigated. Tongue cancers make up 1% of Western malignancies, while the incidence in parts of India is 20%. The peak age incidence in Bombay is in the 40-45 yr age group, while those aged 55-75 yr are more often affected in England and the United States. Males are more often affected than females. Carcinoma of the tongue has been related to various environmental factors, including tobacco chewing, smoking, poor oral hygiene and dental irritation, and alcohol. In 1 study, 77% of patients with tongue cancers were smokers. Iron deficiency and the chronic superficial glossitis involved in tertiary syphilis have also been implicated as etiological factors in carcinoma of the tongue. The prevalent histological type of tongue carcinoma is squamous cell carcinoma, with adenocarcinoma of the salivary glands and metastatic carcinoma being among the rarer diagnoses. Leukoplakia conditions affecting the tongue have been related to carcinoma, with 12% of patients with leukoplakia developing carcinoma in 1 study. Carcinoma of the tongue was located on the anterior portion of the tongue 1.5 times more often than on the basal portion in 1 study, with most lesions being found on the lateral borders of the tongue. In advanced stages, the disease may extend deeply into the tongue musculature, the mandible, palate and larynx. Tongue carcinomas are often multicentric, and there may be a relationship between smoking and the likelihood of developing a second tumor. Lymph nodes are involved in many cases; distant metastases were observed in 5% of the cases in 1 study. Prognosis is directly related to the stage of the disease, and survival has improved in recent years with improvements in diagnostic techniques. (58 references)

0848 THE STIMULATION AND INHIBITION OF HEPATIC MICROSOMAL DRUG-METABOLIZING ENZYMES WITH SPECIAL REFERENCE TO EFFECTS OF ENVIRONMENTAL CONTAMINANTS. (E.) Fouts, J. R. (Coll. Med. U. Iowa, Iowa City). *Toxic Appl Pharmacol* 17(3):804-809, 1970.

Factors that should be considered in determining the stimulatory or inhibitory activity of environmental chemicals on hepatic microsomal drug-metabolizing enzymes and areas of research that have been neglected were noted. The amount of time required before pharmacological activity is detected varies among experiments, different species produce different responses as do the same species receiving the test drug by different routes (p.o., i.p., or s.c.). Inducers often contain inhibitory activity

(while inhibitors frequently cause an induction of the microsomal enzymes), and some test compounds affect only a few microsomal enzymes. Compounds that are rapidly metabolized or excreted must be given repeatedly before activity can be detected, and the effects on steroid metabolism or environmental interactions may be important in determining toxic effects of the compounds. Systems not requiring cytochrome P-450, some environmental toxins (tetraethyl lead), activity in nonhepatic tissues, and interactions between environmental toxins and food additives are relatively neglected areas of study. Additional information is needed on species differences (particularly the primates), on the effects of microsomal enzyme activity alteration on the action of drugs, and on effects of environmental contaminants on renal and biliary excretion. Changes in absorption or tissue and plasma protein binding, as well as the relation of placental structure differences to transfer of materials from mother to fetus should also be investigated. (19 references)

0849 HEPATIC CANCER AND MYCOTOXINS. (Fr.) Le Breton, E. (Cordeliers Sch. Med. Sci., Paris, France) *Ann Biol Clin* 28(3):203-208, 1970.

Reasons for the increase in the incidence of hepatic cancer in humans within recent years in temperate regions which have a high standard of living, as in France, are discussed. The evolution of cirrhosis of the liver toward a cancerous process is attributed to the ingestion of carcinogenic substances in the food such as mold toxins. Among recently discovered carcinogenic mycotoxins are luteoskyrine (from *Penicillium islandicum* which is a rice mold found in the tropical regions of Asia) and the aflatoxins. The latter was discovered by the observation of an acute hepatitis in turkeys after they had ingested some peanut cakes which were found to be contaminated with *Aspergillus flavus*. A number of aflatoxins have been discovered which have been separated chromatographically and their spectra determined under U.V. They were named aflatoxins B₁, B₂ (blue fluorescence) and G₁, G₂ (yellow-green fluorescence). The toxicity of aflatoxin affects all organisms and in the higher animals is manifested mainly in the liver, the toxic doses varying with the species. In the rat hepatocellular changes caused by aflatoxin result in inhibition of nucleic acid synthesis and compensatory hypertrophy of the liver occurs. DNA and RNA metabolism is discussed in this context. (8 references)

0850 ETIOLOGICAL ASPECTS OF SQUAMOUS CANCERS OF THE HEAD AND NECK. (E.) Wynder, E. L. (Amer. Hlth. Found., New York, N.Y.) *Jama* 215(3):452-453, 1971.

Various environmental factors associated with squamous cell cancer of the head and neck were reviewed. A close association has been established between tobacco usage and squamous cell cancer of the head and neck in virtually all sites. Cancer of the vocal cords was found to be predominantly related to cigarette smoking, while other head and neck can-

cers, including cancers of the oral cavity and pharynx, are equally strongly associated with pipe and cigar smoking. Data from India have indicated that tobacco and betel nut chewing is causally related to cancer of the mouth. In women, oral cancer was usually found to be located in the tongue or buccal mucosa. Cancer of the head and neck in sites other than the lip and vocal cord was strongly related to heavy alcohol consumption; however, the fact that most heavy drinkers also smoke made it difficult to assess the relative weights of smoking and drinking as etiological factors for these conditions. While no evidence that alcohol is carcinogenic *per se* exists, it was suggested that alcohol may potentiate the carcinogenic effects of tobacco smoke. Syphilis has been correlated with cancer of the anterior 2/3 of the tongue; and liver cirrhosis has also been correlated with cancer of the upper alimentary tract. The correlation of Plummer-Vinson's disease brought on by iron deficiency and cancer of the squamous tissue of the mouth and pharynx may suggest that cancer of the head and neck are sometimes associated with deficiency conditions. It has been shown that riboflavin deficiency can lead to atrophy and hyperkeratosis in the upper alimentary tract. The skin of riboflavin-deficient mice was found to be more susceptible to carcinogenic agents than the skin of normal mice. Heavy cigarette smoking apparently makes patients more likely to develop a second primary tumor in the oral cavity and upper respiratory tract. Furthermore, cessation of smoking and drinking after the appearance of the first primary tumor did not ensure that a second primary tumor will not develop. (no references)

- 0851 PRECANCEROUS CONDITIONS OF THE ESOPHAGUS. (Fr.) Mounier-Kuhn, P. (no affil), J. Gaillard, J. P. Haguenauer and P. A. Bernard. *J Med Lyon* (1197):1957-1963, 1970.

Precancerous states of the esophagus where the etiology is known or presumed and those of an unknown etiology were investigated. To the first category belong the cicatricial, the atonic wounds, and the inflamed lesions. The agent responsible for scarring is usually caustic soda or a product containing it, and cancer formation, which occurs only years later, is usually located at the stenotic area. This type of cancer may develop from other trauma such as hot food or acids and continuous infection due to stasis. Atonic wounds of the esophagus are more rare; a neoplasm may develop from a previously calcified ganglion. Both the above mentioned states may be regarded as precancerous. The 3 main esophageal syndromes giving rise to inflamed lesions are: peptic stenosis, megaesophagus, and esophageal diverticulum. Precancerous states of indeterminate etiology include: esophageal dysplasia during sideropenia, esophageal leukoplakia, and benign tumors. All these states have in common an esophagitis which favors the development of a cancer. Prophylactic as well as surgical treatment is discussed. (12 references)

- 0852 PATHOGENESIS OF CARCINOMA OF THE UTERINE CORPUS. (Bul.) Ivanov, I. I. (Med. Inst. Sofia, Bulgaria) and V. Makaveeva. *Akush Gynec [Sofia]* 9(5):413-418, 1970.

A review on the specific features in the development of endometrial carcinoma is presented. The interactions between the uterine mucosal epithelial cells and the environmental stroma undergo considerable alterations at the menopausal stage. The turnover of the endometrial epithelial cells occurring during sexual life ceases and the static conditions of these cells render them a susceptible target to endogenous carcinogenic factors generated by hormonal disorders. Thus the uterine mucosal epithelium becomes a potential site for malignant transformation. (14 references)

- 0853 THE GENESIS OF SOME EPITHELIAL CHANGES, SOMETIMES PRECEDING OR ATTENDING THE APPEARANCE OF CANCER OF THE CERVIX UTERI: A REVIEW OF COMPARATIVE AND EXPERIMENTAL DATA. (E.) Volfson, N. I. (Ministry Publ. Hlth., Leningrad, USSR). *Neoplasma* 17(5):541-555, 1970.

Intraepithelial cervical changes preceding or attending the appearance of invasive cancer of the cervix uteri that have been investigated are reviewed. The development of apparently immature endocervical stratified squamous epithelium (in the fourth decade of a woman's life, during pregnancy, and in the newborn) results from excessive estrogenic stimulation; the newly formed stratified squamous epithelium of infancy, childhood, and senility is identical to the normal mature stratified ectocervical epithelium (and may be derived from it). Hyperplasia of reserve cells, dysplasia, and carcinoma *in situ* of the cervix uteri display identical histogenesis, and the morphology in the cervical epithelium may reflect normal age-determined processes as well as certain pathological processes (carcinogenesis of the cervix uteri). (95 references)

- 0854 MALIGNANT TRANSFORMATION OF CELLS CULTIVATED *IN VITRO*: A MODEL OF CARCINOGENESIS WITH SPECIAL REFERENCE TO "SPONTANEOUS" MALIGNANT TRANSFORMATION. (E.) Briand, P. (Fibiger Lab., Kongens Lyngby, Denmark). *Danish Med Bull* 17(8): 217-225, 1970.

The metabolic, morphological, and growth characteristics of cells undergoing malignant transformation *in vitro* were reviewed. The architectural appearance of malignant cells *in vitro* may be distinctive; elongated spindle-shaped cells growing in several layers and forming aggregations have been found to be characteristic of malignant cells. In human cells, shifts from diploidy to heteroploidy have been found in association with malignant transformation. Changes in ploidy have been associated with malignant transformation in other cell systems. In cell cultures *in vitro*, growth

proceeds in phases: an initial proliferative stage, followed by a stage of sluggish growth, followed by a stage of rapid proliferation. The final phase has been suggested as being indicative of malignant transformation in human cell cultures. A characteristic feature of cancer metabolism is the large lactate accumulation; malignancy has also been found to be accompanied by increased glycogen metabolism in some tissue cultures. Glycolytic metabolism is usually associated with the initial phase of cell growth *in vitro*, while the final phase of rapid proliferation is marked by chromosomal changes. Whether malignant properties arise in the later phase is unclear; the changes observed in the various phases of cell growth may be either causes of malignant transformation or effects of prior malignant transformation. (86 references)

0855 CHEMICAL MUTAGENS AS A POSSIBLE GENETIC HAZARD IN HUMAN POPULATIONS. (E.) Malling, P. V. (Oak Ridge Natl. Lab., Tenn.). *Amer Indust Hyg Ass J* 31(6):657-666, 1970.

Mutagenic chemical compounds, their uses by man, and their mutagenic pathogenicity in experimental systems were reviewed. Mutagenic compounds may produce lethal dominant or lethal recessive mutations, or may affect the morphology of the organism ingesting it without killing that organism. Two widely-used experimental systems for testing the mutagenicity of compounds are neurospora and mice, in which the production of dominant lethal mutations may be conveniently tested. Highly mutagenic chemical compounds include ethyl and ethyl methanesulfonate, which induce dominant lethals in mice, and N-methyl-N'-nitro-N-nitrosoguanidine, which is highly mutagenic and carcinogenic. Other chemical mutagens include 2-methoxy-5-chloro-9-[3-(ethyl-2 chloroethyl)aminopropylamino]-2,4,6-tris(1-aziridinyl)-1,3,5-triazine which induces nuclear-killing chromosome deletions and point mutations in neurospora. Mutagenic chemicals having widespread use in the human environment include nitrites and nitrates, some insecticides and herbicides, some antimalarial, anti-neoplastic, and antibiotic drugs (including Actinomycin D), and caffeine. The increasing use of mutagenic agents by men indicates that there is a risk of increasing genetic disease in the human population, although it is not always possible to extrapolate from known mutagenic effects on laboratory animals to mutagenic effects on men. (47 references)

0856 SPONTANEOUS CHROMOSOMAL BREAKAGE AND HIGH INCIDENCE OF LEUKEMIA IN INHERITED DISORDERS. (E.) Schroeder, T. M. (Inst. Anthro., Human Genet., U. Heidelberg, Germany) and R. Kurth. *Blood* 37(1):96-112, 1970.

The association between chromosomal breakage and high leukemia incidence which has been observed in several diseases was reviewed; the diseases were ataxia telangiectasia, Bloom's syndrome, Fanconi's anemia, glutathione reductase deficiency, Kostmann's agranulocytosis, and pernicious anemia. In these diseases, the incidence of chromosomal aberrations,

including achromatic regions, chromatid and chromosome breaks, fragments, translocation figures, rings and dicentrics is high; and in all these diseases, it has been observed that patients contracting them are unusually likely to contract leukemia. A relation between chromosomal anomalies observed *in vitro* and hematological disorders *in vivo* has been shown for Fanconi's anemia and in glutathione reductase deficiency; this relationship depends on the stage of the disease, anomalies being restricted to immature red cells only when the disease involves the erythropoietic system. No *in vivo* studies have been performed on the relationship between *in vitro* and *in vivo* states in Bloom's syndrome or ataxia telangiectasia. In Kostmann's agranulocytosis, chromosome breakage has been demonstrated *in vivo* only. Culture conditions obscure the relation between *in vitro* findings and *in vivo* events in pernicious anemia. Apparently, many instances of negative findings for chromosomal abnormalities associated with these conditions are misleading and ignore evidence of abnormalities. Chromosomal breakage *in vitro* and *in vivo* is apparently the result of a primary genetically determined defect whose precise nature is unknown. The possibility that the cells are influenced *in vitro* to abnormal development remain. (88 references)

0857 THE ROLE OF MIGRANT POPULATION IN STUDIES OF SELECTED CANCER SITES: A REVIEW. (E.)

Kmet, J. (Int. Agency Res. Cancer, Lyon, France). *J Chron Dis* 23(5-6):305-324, 1970.

The incidence of cancer of various sites in migrant populations, as compared to incidences in stationary populations, was reviewed. Most of the data has been compiled on immigrants to the United States. Oral cancer rates are higher for Irish migrants to the U.S. than for Russian migrants, a finding which may relate to the role in oral cancer of excessive alcohol consumption. A high rate of oral and pharyngeal cancer for Swedish female migrants correlated with a high rate of cancer in these sites for native Swedish females as compared to males. All foreign-born males in one study had higher rates for esophageal cancer than did native born American males, while incidences for migrant females were more variable. Immigrant male Poles had mortality rates from esophageal cancer more than twice as high as non-immigrant males in Poland and in the U.S. Stomach cancer rates in all ethnic groups in the U.S. were higher than those for the native white population, highest risks being found for migrants from Poland and Czechoslovakia. Incidence rates for cancer of the large intestine and rectum among people migrating within the U.S. correlated more closely with rates for regions of most recent residence than with rates for regions of birth. Risks for colon and rectal cancer among Polish immigrants differed from risks incurred by the native Polish population, and conformed to those incurred by U.S. residents. No striking departure from native U.S. incidence rates for prostatic cancer or cancer of the ovary were found for migrant groups. Migrants from countries having higher or lower lung cancer rates than the U.S. showed lung cancer incidence

rates intermediate between those of the native country and the U.S. Immigrants to the U.S. from Russia, especially Jewish immigrants, showed an excess risk for leukemia. (52 references)

0858 SOME INTERCOUNTRY AND INTERGROUP DIFFERENCES IN HISTOLOGICAL TYPES OF CANCER. (E.)

Berg, J. W. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.). *J Chron Dis* 23(5-6):325-334, 1970.

Relationships in various geographic areas between the incidence and the histological origin of different carcinoma conditions were investigated in a survey of the available literature. Adenocarcinomas of the stomach may be distinguished into the diffuse and the intestinal type; the latter predominates in high-incidence areas in Latin America. Bantu people with low incidences of bowel cancer have relatively more colloid carcinomas. Mesotheliomas of the pleura and peritoneum are extremely rare, except in association with asbestosis, where they are common; and nasal and sinus adenocarcinomas are of high incidence among furniture workers exposed to wood dust. Cystosarcomas of the breast are more frequent in the Orient, while medullary and colloid carcinomas are more common in Japan. In England, seminomas of the testis are found in excess in rural areas, while other tumors are no more frequent in the country than in towns. Bantus were found to have a low incidence of gliomatous brain tumors compared to whites; however, they develop meningiomas at the same rate as whites. Negro children in the United States appear to be less susceptible to acute lymphatic leukemia than whites. (46 references)

0859 OIL AND CARCINOMA OF THE SCROTUM. (E.)

Kipling, M. D. (no affil). *Trans Soc Occup Med* 19(2):36-40, 1969.

The association of carcinoma of the scrotum with occupational exposure to mineral oils, and the incidence and pathology of carcinoma of the scrotum were reviewed. The association between cancer of the scrotum and mineral oils used in the textile industry and in the petroleum fuel industry in England is of long-standing documentation. The major risk of exposure today is in engineering or machining work, in which oils are used in connection with the cutting and milling of metals. Oils which have not been solvent-refined are more apt to induce carcinoma of the scrotum than oils which have been solvent-refined. The actual agent in cutting oils which causes carcinoma of the scrotum has not been identified, but the aromatic hydrocarbons may be implicated. Prolonged contact with oil and lack of personal cleanliness are predisposing factors for scrotum carcinoma. Age apparently does not influence risk of developing carcinoma of the scrotum; patients observed ranged in age from 8-91 yr. Working conditions, including heat, humidity, and high speed of the spindle to which the oil is applied as a lubricant, may also potentiate the carcinogenic effects of mineral oils. The incidence of carcinoma of the scrotum shows no signs of increasing; in Birmingham, England, 58 deaths from

carcinoma of the scrotum were recorded between 1958-1965 in a total population of 5 million. Carcinoma of the scrotum has a poor prognosis, with only 8 of 27 patients in 1 study surviving for 5 yr after initial treatment. Carcinoma of the scrotum ordinarily begins its course as a epithelioma which may later develop into a malignant lesion and at times invades the testicles. (36 references)

0860 ENZYMATIC REGULATION OF THE PLASTICITY OF THE ORGANISM AND CARCINOGENESIS. (Rus.)

Rapoport, I. A. (Inst. Chem. Physics Acad. Sci. USSR, Moscow), V. A. Parnes and D. M. Kevin. *Pat Fiziol Eksp Ter* 16(5):56-62, 1970.

The role of mutation and dedifferentiation in the pathogenesis of oncogenic processes is critically analysed. Reference is made to genetic studies with *Drosophila melanogaster* subjected to oncogenic RNA (Defective and nondefective strains of rous virus) and DNA (polyoma strains of the papova and human adenovirus type 12) viruses. None of these viruses produced genetic alterations under appropriate experimental conditions, thus contradicting results obtained by other authors. Therefore a mechanism of modification operating by means of a set of basic enzymes is suggested to be instrumental in neoplastic pathogenesis. This set of basic or operative enzymes would participate in the elaboration of products both inert and active in determining the concentrations of key substances such as nucleic acids and amino acids, and would control the initial stages of mitosis. Removal of such an operative enzyme from the metabolic framework in the adult organism may lead to uncontrolled cell proliferation. When the deviation due to the block of such an enzyme controlling cell division is of a limited nature, cell proliferation characteristic for benign neoplasia may occur. In cases in which a highly developed synthetic system loses an enzymatic factor controlling mitosis, malignant neoplastic growth may occur. In such case mobilization of energetic resources throughout the whole organism would take place. The continuity of the modification process would be maintained because the loss of such a controlling enzyme would not lead to cell death but to cell proliferation. (22 references)

0861 MALIGNANT TUMORS AMONG TWINS: A STUDY OF DIVERGENT VIEWS. (E.) Keith, L. (Chicago

Med. Sch., Ill.) and E. Brown. *Acta Genet Med Gemellol* 19(4):576-583, 1970.

The tendency of both members of dizygotic and monozygotic twins to develop cancer was investigated in a review of the literature of the subject. Most studies agreed that monozygotic twins have higher concordance rates for cancer than dizygotic twins. Especially high concordance rates have been reported for mammary cancer, uterine cancer, gonadal cancer, cancer in the eye, stomach cancer, and rectal cancer. Tumors, including type, site, and age of onset, appeared to affect monozygotic twins more than both members of a dizygotic twin pair. The

precise nature of the genetic effect on tumorigenesis in twins remained in doubt, although a mechanism for cancer concordance among monozygotic twins probably does exist. Confident conclusions about the development of cancer in twins is impeded by the diversity of patient groups, lack of standardization of collected data, and unreliability of classifications of mono- or dizygosity. (46 references)

62 HISTOGENETIC STUDY OF THE BASAL CELL EPITHELIOMA. (E.) Kint, A. (Dept. Derm. U. Gent, Belgium). *Curr Probl Derm* 3:82-123, 1970. (4 references)

63 BIOLOGICALLY ACTIVE BENZO(b)THIOPHENE DERIVATIVES. (E.) Campaigne, E. (Chem. Lab. Indiana U., Bloomington), D. R. Knapp, E. S. Neiss and T. R. Bosin. *Advances Drug Res* 5:1-54, 1970. (76 references)

64 THE GENETICS OF ANIMAL VIRUSES. (E.) Fenner, F. (John Curtin Sch. Med. Res., Australian Natl. U., Canberra). *Ann Rev Microbiol* 24:297-334, 1970. (264 references)

65 POLYNUCLEAR AROMATIC HYDROCARBONS IN THE WATER ENVIRONMENT. (E.) Andelman, J. B. (Grad. Sch. Publ. Hlth., U. Pittsburgh, Pa.) and M. Suess. *Bull WHO* 43(3):479-508, 1970. (252 references)

66 VIRUS-INDUCED CHROMOSOME ABNORMALITIES. (E.) Nichols, W. W. (Inst. Med. Res., Camden, N. J.). *Ann Rev Microbiol* 24:479-500, 1970. (64 references)

67 LEUKEMIA AND VIRUSES: INTRODUCTION TO THE RESEARCH ON VIRAL ETIOLOGY OF HUMAN LEUKEMIA. (Jap.) Kuwata, T. (Sch. Med. Chiba U., Japan). *Chiba Med Soc* 46(2):141-148, 1970. (35 references)

68 FEATURES IN THE EPIDEMIOLOGY OF NEOPLASTIC DISEASE. (Dan.) Clemmesen, J. (Inst. Cancer Epidemiol., Denmark). *Ugeskr Laeg* 132(50):2403-2411, 1970. (17 references)

69 ONCOLOGY AND GERIATRICS. (Sp.) Vicente, J. (Dept. Oncol., Jimenez Diaz Found., Madrid, Spain). *Rev Clin Espagn* 119(2):103-110, 1970. (34 references)

0870 BURKITT'S LYMPHOMA. (Fr.) Bonnet-Gajdos, M. (Hosp. Trousseau, Paris, France), J. Boulesteix and J. L. Fontaine. *Vie Med* 51(37):5099-5110, 1970. (7 references)

0871 HORMONAL CONTRACEPTIVES. (Sp.) Martinez-Manautau, J. (Dept. Sci. Invest., I.M.S.S., Mexico City) and J. Giner. *Gac Med Mexico* 100(10):993-1026, 1970. (186 references)

0872 THE ETIOLOGY OF BRONCHIAL CARCINOMA. (Dut.) Gyselen, A. (no affil). *T Geneesk* 26(23):1121-1214, 1970. (No references)

0873 THE EPIDEMIOLOGY OF CANCER. (Dut.) Vandendriessche, R. (no affil). *T Geneesk* 26(23):1183-1188, 1970. (No references)

0874 THE EFFECT OF GLASS FIBERS ON THE LUNG. (Ger.) Wewer, B. (Tech. Coll. Aachen, Germany). *Lebensversicherungsmedizin* 22(6):125-127, 1970. (19 references)

0875 VIRUS AND LYMPHOMA. (Fin) Saksela, E. (Clin. Pathol. Lab. Helsinki, Finland). *Duodecim* 86(16):880-885, 1970. (13 references)

0876 RECENT PROGRESS IN THE STUDY OF PROLIFERATIVE KINETICS IN ACUTE LEUKAEMIA. (It.) Masera, P. (Med. Clin. U. Turin, Italy), V. Gabutti and F. Gavosto. *Minerva Med* 61(88):4965-4972, 1970. (27 references)

0877 THE ACTION OF ENVIRONMENTAL AND OCCUPATIONAL FACTORS ON THE ETIOLOGY OF MALIGNANT TUMORS. (It.) Leone, G. (no affil). *Minerva Med* 61(88):5006-5012, 1970. (28 references)

0878 OCCUPATIONAL TUMORS. (It.) Cesaro, A. N. (Inst. Med. Lavoro, U. Messina, Italy). *Recent Progr Med* 49(3):258-290, 1970. (no references)

0879 SMOKED FOOD PRODUCTS AND CARCINOGENESIS. (Fr.) Lederer, J. (no affil). *Louvain Med* 89(9):607-610, 1970. (23 references)

0880 CARCINOGENIC COMPOUNDS IN SPINACH. (Ger.)
Schmidt, F. (Res. Inst. Prevent. Oncol.,
Mannheim, U. Heidelberg, Germany). *Munch Med Wschr*,
112(45):2056, 1970. (7 references)

0881 STUDIES ON THE DETERMINATION OF AFLATOXINS.
(Ger.) Bösenberg, H. (Hyg. Inst. Westphal-
ian Wilhelms U., Munster, Germany). *Arzneimittel-
forschung* 20(10):1521-1528, 1970. (251 references)

0882 EFFECT OF VIRUS INFECTIONS ON THE FUNCTION
OF THE IMMUNE SYSTEM. (E.) Notkins, A. L.
(natl. Inst. Dent. Res., Natl. Inst. Hlth., Bethesda,
Md.), S. E. Mergenhagen and R. J. Howard. *Ann Rev
Microbiol* 24(525-538, 1970. (121 references)

0883 MODERN VIEWS ON CARCINOGENESIS. (Dut.)
Vandeputte, M. (no affil). *T Geneesk*
26(23):1189-1193, 1970. (No references)

CHEMICAL CARCINOGENESIS

0884 BRONCHIAL EPITHELIAL ALTERATIONS AND PULMONARY NEOPLASIA INDUCED BY OZONE. (E.)

Werthamer, S. (Methodist Hosp. Brooklyn, N. Y.), L. H. Schwarz and L. Soskind. *Path Microbiol* 35(1-3): 224-230, 1970.

The effect of ozone in air at sublethal concentrations on tumor resistant mice (male Swiss Webster) was studied with and without desmosterol treatment. One group of 100 mice was exposed to 4.5 ppm ozone in air for 2 hr every 3rd day for 75 days and received daily injections of desmosterol (0.2 mg). Another group of 120 animals were exposed to ozone on the same schedule as the first group and received daily injections of saline. A third group of 55 mice served as controls; 54 of these animals exhibited normal lung morphology at sacrifice, while one animal showed a mild focal hyperplasia of the bronchial epithelium. The experimental animals were randomly sacrificed from the 6th day on. Edema, congestion, scattered hemorrhage, bronchiectasis, emphysema, bronchitis, bronchiolitis, bronchopneumonia and microabscesses were the progressive changes observed with increasing numbers of exposure to ozone. Of the mice treated with ozone and desmosterol, 38% exhibited cellular changes, while 23% of the mice exposed to ozone and saline showed cellular changes. These changes ranged from hyperplasia, atypism, pyknotic and hyperchromatic nuclei to metaplasia and adenoma formation (8.0 and 6.6% for the ozone-desmosterol and ozone-saline-treated mice, resp.).

0885 PROSTATIC HYPERPLASIA AND NEOPLASIA IN FEMALE *PRAOMYS (MASTOMYS) NATALENSIS*. (E.)

Holland, J. M. (Northwestern U. Med. Sch., Chicago, Ill.). *J Nat Cancer Inst* 45(6):1229-1236, 1970.

Hyperplasia and neoplasia (associated with androgen injections) in the prostate of the female *Praomys (Mastomys) natalensis* were investigated. Proliferative changes in the prostate were found in 16 untreated controls; the changes became increasingly marked with age. In controls over 24-months-old, papillary hyperplasia was often seen, usually with granulosa cell proliferation of the ovary and proliferative changes of the endometrium. In all 18 *Mastomys* treated with testosterone injections (5 mg s.c. pellets of testosterone propionate every 3 wk or 10 mg i.m. of testosterone enanthate every 3 wk), the prostate became enlarged, and marked papillary hyperplasia developed with prolonged testosterone treatment. None of the androgen-treated *Mastomys* developed prostatic neoplasms. Ovine prolactin (8 mg pellet s.c. every 3 wk) administered with or without testosterone had no effect on prostate, body wt or other organs. Cystic dilatation was observed in 2 of 4 animals given diethylstilbestrol (12 mg pellet s.c. every 2 months). Solid adenomatous proliferation occurred in both of 2 untreated animals (26 months-old) with malignant prostatic changes and probable granulosa cell proliferation of the ovary.

0886 INFLUENCE OF HYPOTHYROIDISM ON THE DEVELOPMENT OF NEOPLASTIC PROCESSES IN RAT MAMMARY GLAND. (Rus.)

Skatkov, M. E. (Inst. Med. Genetics Acad. Med. Sci. USSR, Moscow) and V. I. Romanov. *Biull Exp Biol Med* 70(11):93-95, 1970.

The effect of 6-methylthiouracil (MTU) on the formation of mammary gland tumors was studied in 133 randombred female Wistar rats (120 g wt) divided into 3 experimental groups: 1) 42 rats were given 10 mg MTU in the diet daily for 2 yr; 2) 41 rats received the same dose daily with 30 day intervals for 2 yr; 3) 50 rats constituted the control group. An additional 9 rats were thyroidectomized and subjected to a count of gonadotropic (estrogen-secreting) cells in the adenohypophysis 8 days later. Continuous administration of MTU produced tumors in 17 rats, 8 of which had mammary gland adenocarcinoma, 1 had mammary gland hyperplasia, 3 had lung cancer, 2 had liver cancer and 1 had tumors of the ovaries. Intermittent administration of MTU produced tumors in 7 rats, 6 of which had cancer of the mammary gland, and 1 rat had liver sarcoma. The thyroidectomized rats exhibited approximately 9% levels of basophilic estrogen-secreting cells in the adenohypophysis and the intact control rats had 7% of such cells. The data seem to support the hypothesis that hyperestrinism is involved in development of hyperplasia and mammary gland cancer.

0887 THE INFLUENCE OF THYROACTIVE SUBSTANCES ON THE INDUCTION OF CERVICO-VAGINAL TUMORS IN INTACT AND CASTRATE RATS. (E.)

Cherry, C. P. (Strange-ways Res. Lab., Cambridge, England) and A. Glucksmann. *Brit J Cancer* 24(3):510-527, 1970.

The effect of L-thyroxine and of methylthiouracil on the development and incidence of cervico-vaginal tumors induced by 7,12-dimethylbenz(a)anthracene (DMBA) was investigated in intact and castrated rats. Rats were given L-thyroxine alone (20 µg in drinking water), with methylthiouracil (20 mg in drinking water) or, with stilbestrol (2 µg). DMBA (1%) was administered topically at weekly intervals. Methylthiouracil accelerated the rate of sarcoma induction in intact rats, while methylthiouracil with L-thyroxine delayed the appearance of tumors and reduced their numbers. Perinatal injections of either L-thyroxine or methylthiouracil in intact rats delayed the appearance of tumors. L-Thyroxine, methylthiouracil, or combinations of either agent with stilbestrol accelerated sarcoma production and increased the numbers of developing sarcomas in castrated rats. L-Thyroxine and methylthiouracil accelerated the development of tumors, but did not increase their numbers. Methylthiouracil accelerated and increased the numbers of epithelial tumors in both intact and castrates; this effect was reduced by stilbestrol treatment and L-thyroxine with methylthiouracil treatment in intact rats and was potentiated in castrates. Untreated castrates had higher incidences of sarcomas than untreated intact rats or intact rats given L-thyroxine and stilbestrol; the incidence of epithelial tumors was low in both untreated castrates and intact rats and greater in castrated than in intact rats given methylthiouracil with stilbestrol or L-thyroxine. Changes in the thyroid and the hypophysis induced by the 2 agents were not related to carcinogenesis. The differing responses of castrates and intact rats to tumor induction by the agents may be due to local factors.

0888 TUMOUR-PROMOTING PROPERTIES AND METABOLISM OF 5α-CHOLEST-6-ENE AND 5α-CHOLESTA-1,3,6-TRIENE. (E.)

De Kock, D. H. (Dept. Chem. U.

Stellenbosch, Union South Africa) and J. H. Barnardt. *S Afr Med J* 44(44):1274-1276, 1970.

The tumorigenic efficacy and the metabolism of 2 derivatives of cholesterol, 5 α -cholest-6-ene, and 5 α -cholesta-1,3,6-triene, were studied in mice. Male mice were injected s.c. with either of the 2 agents in combination with dibenz(a,h)anthracene (DBA) for varying periods of time. Of 12 mice given DBA (0.1 mg) alone, 3 developed tumors by 28 wk after injection, and 7 developed tumors by 50 wk postinjection. Of 10 mice given DBA (0.1 mg) and 5 α -cholest-6-ene (20 mg), all had developed tumors by 28 wk postinjection. The same results were obtained in mice given DBA and 5 α -cholesta-1,3,6-triene. Mice given only the cholesterol derivatives developed tumors in only 1 of 40 cases 50 wk after postinjection. Metabolic studies showed that 5 α -cholest-6-ene was metabolized to 5 α -cholestane-6 β , 7 α -diol, which was conjugated with glucuronic acid. The 5 α -cholesta-1,3,6-triene was converted to the glucuronide of 5 α -cholesta-1,3-dien-6 β , 7 α -diol. Enzymes responsible for this conversion were located in liver microsomes and required NADPH as a co-factor. The steroidal hydrocarbons may exert their tumorigenic effects by blocking the detoxification of DBA.

0889 EFFECT OF ALTERED HORMONAL STATES ON THE HISTOCHEMICAL DISTRIBUTION OF NUCLEIC ACIDS IN THE RAT PROSTATIC COMPLEX. (E.) Takkar, G. L. (Central Drug Res. Inst., Lucknow, India), V. P. Kamboj and A. B. Kar. *Indian J Exp Biol* 8(2): 63-67, 1970.

The effect of progesterone, estrogen, and altered thyroid status on the cytochemical distribution of DNA and RNA in the rat prostate was investigated. Rats were given 1 and 2.5 mg progesterone or 0.1 and 5 μ g estradiol by s.c. injections daily for 15 and 30 days. Progesterone evoked a progressive increase in intensity of the Feulgen staining reaction; the intense staining of the nuclei of epithelial and stromal cells appeared to be related to an increase in their chromatin content. Progesterone also increased both DNA and RNA contents of epithelial, stromal, vascular and mast cell elements. Cytoplasmic and nuclear RNA of the acinar epithelium increased after progesterone treatment more prominently in the ventral and lateral prostate. At low doses of estrogen, DNA and RNA in the nuclei, nucleoli, and cytoplasm of the acinar epithelia, stroma, blood vessels and mast cells were elevated. The higher dose of estrogen significantly inhibited prostatic function; the acinar epithelium was metaplastic and there was no secretion in the lumen. The stroma was hypertrophied and hyperplastic. DNA contents of epithelial chromatin, stromal and vascular elements increased markedly, while RNA levels increased only slightly. A combined dose of progesterone and estrogen produced results which were thought to suggest that the estrogen effect was antagonized by progesterone. In rats which had been thyroidectomized, prostatic function seemed to be stimulated; DNA content of chromatin of the epithelial cells was reduced in these rats.

0890 UPTAKE AND LOSS OF TRITIATED OESTRADIOL BY THE ADRENAL GLAND AND BY OESTROGEN-INDUCED ADRENOCORTICAL CARCINOMA IN THE RAT. (E.) Mobbs, B. G. (Dept. Urol., Queen's U., Kingston, Ontario, Canada). *J Endocr* 48(4):545-552, 1970.

The retention of estradiol by adrenals and tumors in rats with estrone-induced adrenocortical tumors and by adrenals in tumor-free rats was investigated. Female rats bearing estrone-induced tumors were used; 1 group carried tumors which grew only in rats bearing estrone pellets, and another group carried tumors which grew more quickly in rats with estrone pellets. Estrone-induced tumors were transplanted to ovariectomized rats without estrone pellets. All rats were given s.c. injections 16.7 μ C 6,7-³H-estradiol-17 β ; tritiated estradiol was also injected into non-tumor bearing rats (controls). In the adrenals of controls, uptake and loss of estradiol was rapid; there was no evidence of specific retention of the hormone by the adrenal. Mature ovariectomized non-tumor bearing rats retained 287.5 cpm of tritiated estradiol 150 min after injection, while retained estradiol for immature and mature but not ovariectomized rats at 150 min postinjection were 59 and 312 cpm, resp. Adrenals retained more estradiol than muscle in all cases, with ratios of estradiol retained by adrenals to estradiol retained by muscle ranging from 11:1-7:6. In rats bearing the tumor which grew only in the presence of estrogen, patterns of loss of estradiol were similar. At 23 min postinjection, the adrenals retained 147.9 cpm estradiol, while by 183 min postinjection, retention was down to 15.7 cpm. Retention of estradiol by the adrenocortical tumor was similar to retention by the adrenals. In rats bearing the tumor which grew more rapidly in the presence of estrone, retention of tritiated estradiol was at the level of 175 cpm in the adrenal (188 cpm in the tumor) at 36 min postinjection; by 179 min, 84 cpm of estradiol was retained in the adrenal (68 cpm in the tumor). In this tumor line, loss of estradiol from the host adrenal and the tumor was slower than that from muscle, while in the former tumor line there was no significant differences in the loss of estradiol by these systems. Loss of estradiol may have been determined more by the hormonal environment of the tissues than by estrogen receptors in the adrenal.

0891 EFFECT OF 17- β -ESTRADIOL AND TESTOSTERONE ON ARYL HYDROCARBON HYDROXYLASE ACTIVITY IN MOUSE TISSUES *IN VIVO* AND IN CELL CULTURE. (E.) Nebert, D. W. (Natl. Inst. Child Hlth., Human Develop., Natl. Inst. Hlth., Bethesda, Md.), L. L. Bausserman and R. R. Bates. *Int J Cancer* 6(3): 470-480, 1970.

The effect of 17- β -estradiol on the induction of the aryl hydrocarbon hydroxylase system by 3-methylcholanthrene (MC) or 7,12-dimethylbenz(a)-anthracene (DMBA) was studied *in vivo* in mouse liver and skin, in mouse fetal cell cultures, and in a cell-free *in vitro* system. Estradiol implants (20 mg, s.c.) did not significantly decrease the hepatic aryl hydrocarbon hydroxylase activity in either the Swiss mice (from 90 to 57 U/mg protein)

the C57BL/6N mice (from 88 to 71 U/mg protein); (2 mg, i.p.) produced a 2- to 4-fold induction of the hydroxylase system 48 hr after injection of DMBA (2 mg, i.p.) did not induce the enzyme. Estradiol did not significantly affect the basal enzyme level (0.013 and 0.040 U/mg protein) in the Swiss or C57BL/6N mice, resp., and did not alter the inducibility of hydroxylase activity by MC (16 µg, topical application) which produced a 4- to 15-fold increase in Swiss mice and a 15-fold increase in C57BL/6N mice, or by DMBA (16 µg, topical application) which produced 4-fold and 2-fold increases, resp., in the 2 strains of mice. In fetal cell cultures (uncomplicated by environmental stimuli) high concentrations of estradiol (1 mM) prevented hydroxylase induction by the polycyclic hydrocarbons; this suggested that physiologic levels of estradiol have little effect on hydroxylase induction and that the mechanism by which estradiol inhibits the skin tumorigenesis by DMBA is not related to this process. *In vitro* studies indicated that both estradiol and testosterone are competitive inhibitors of polycyclic hydrocarbon hydroxylation, estradiol being 10 times more effective than testosterone.

92 THYMIDINE INCORPORATION INTO HeLa CELLS INCREASED BY TUMOR-PRODUCING CROTON OIL FACTOR TPA. (E.) Freienstein, C. (German Cancer Res. Ctr., Heidelberg), S. Freienstein, G. Kreibich, Kinzel and R. Süß. *Naturwissenschaften* 57(12): 5-676, 1970.

HeLa cells treated with 13-0-tetradecanoyl-phorbol-13-acetate (TPA) were transferred into fresh medium, and thymidine incorporation after the medium change was followed to see if release of TPA inhibition would result in overshooting DNA synthesis due to release of a pre-S-phase block by TPA. Twenty-four old HeLa cell cultures were incubated for 24 hr with 10^{-4} - 10^{-10} M TPA in 0.5% dimethylsulfoxide; a TPA-free medium was then substituted and 1 hr thymidine pulses were introduced at 0, 2, 4 and 8 hr. The reaction was stopped at 0°C with trichloroacetic acid precipitation and thymidine incorporation was determined. The peak of overshooting DNA synthesis was a 2-fold increase in thymidine incorporation over control at 8 hr with 10^{-6} - 10^{-7} M TPA; at the 4 hr pulse, the peak thymidine incorporation was 130% of control at the same concentration. The *in vivo* tumor promoting effect of croton oil may be due to a blocking of DNA synthesis which on release results in overshooting DNA synthesis.

93 THE LEUKEMOGENIC ACTION OF PHORBOL. (E) Berenblum, I. (Weizmann Inst. Sci., Rehovot, Israel) and V. Loni. *Cancer Res* 30(11): 2744-2748, 1970.

The carcinogenic potency of phorbol was investigated in mice which were given phorbol alone and in conjunction with 7,12-dimethylbenz(a)anthracene (DMBA). Female mice were divided into 4 treatment groups: 1 group was given a single topical application of DMBA (0.25 mg) together with twice weekly i.p. injections of phorbol (totaling 8-12 mg);

another group was given phorbol without DMBA; a third group was given DMBA without phorbol; and the remaining group comprised the untreated controls. No skin tumors developed in any of the mice in any of the groups. Of the mice given DMBA and phorbol, 70% developed leukemia and 5% developed reticulum cell sarcoma after mean latencies of 118 days for sarcoma and 168 days for leukemia. In the group given phorbol alone, 57% of the mice developed leukemia and 29% developed reticulum cell sarcoma after mean latencies of 196 days for leukemia and 207 days for sarcomas. Mice receiving DMBA alone developed no leukemia, but 4% developed sarcomas, while 6% of the untreated controls developed leukemia and 20% developed sarcomas. Most of the induced tumors were of lymphoblastic origin and nonthymic. Most leukemias showed advanced infiltration of affected organs.

0894 STUDIES ON THE IMMUNE RESPONSES OF BALB/c MICE DURING TUMOR INDUCTION BY MINERAL OIL. (E.) Kripke, M. L. (Hebrew U. Hadassah Med. Sch., Jerusalem, Israel) and D. W. Weiss. *Int J Cancer* 6(3):422-430, 1970.

The effects of mineral oil injections on the immunological responses of BALB/c mice, which are susceptible to the oncogenic effects of oil, and of C57Bl mice, which are resistant, were investigated. Male mice of the 2 strains were given 3 i.p. injections of 0.5 ml of bayol 55 or primol 355, followed by tests of neutralization of bacteriophage T₂, graft-versus-host reaction tests, tests of syngeneic tumor growth, and tumor immunogenicity tests. Although BALB/c mice showed evidence of preneoplastic development between 18-105 days after injection, C57Bl mice showed no signs of neoplastic development. Only a slight decrease was noted in the primary antibody responses against T₂ phage cells of oil-treated BALB/c mice after a single injection. However, there was a marked reduction in the antibody response in these mice after 2 or 3 treatments; no significant reduction was seen in anti-T₂ titers in oil-treated C57Bl mice at any point. In graft-host reaction studies spleen cells from oil-treated and normal mice were injected into newborn (BALB/c x C57Bl)_{F1} hybrids. The mean spleen index of hybrids given cells from BALB/c mice treated twice with oil was lower than that of hybrids given cells from BALB/c donors not treated with oil. In hybrids given cells from C57Bl mice a similar reaction was seen; however, after the 3rd injection of spleen cells, the mean index in these recipients was higher than that of recipients of cells from C57Bl mice not treated with oil. In tests of syngeneic tumor growth, oil-treated mice were given injections of 5×10^3 cells of the oil-induced plasmacytoma MO-8; oil-treated mice were more susceptible to tumor cells than untreated mice. C57Bl mice treated with oil were highly resistant to tumor implantation. Immunogenicity studies on tumors induced by mineral oil in BALB/c mice showed that tumors induced in these mice by oil-injection possessed tumor-associated antigenicity. The results appeared to suggest that immunological depression in the susceptible BALB/c mice may contribute to the development of progressive neoplasia induced by mineral oil.

- 0895 HIGH INCIDENCE OF PULMONARY TUMORS IN dd MICE BY A SINGLE INJECTION OF CYCASIN. (E.) Hirono, I. (Gifu U., Sch. Med., Japan) and C. Shibuya. *Gann* 61(5):403-407, 1970.

The induction of lung and liver tumors in mice treated with cycasin (8-D-glucosyloxyazoxymethane) was investigated. Newborn mice were given a s.c. injection of 0.5 mg cycasin/g body wt (group I) or of 1.0 mg cycasin/g body wt (group II). Of 39 mice in group I, 17 survived more than 150 days after injection, and 88% of the survivors developed lung adenomas and 64% developed liver adenomas and hepatomas. Lung tumors developed from 5-14 months after injection, and liver tumors developed from 7-14 months after injection. Of 115 mice in group II, 57 survived for 16 days after injection; of these 57, 22 showed neurological disorders. Of the 35 mice in group II surviving beyond 150 days post-injection, 83% developed lung tumors (5 carcinomas) and 37% developed liver cell adenomas and hepatomas. Other tumors occurring in group II were reticulum cell neoplasm and leukemia (1 case of each). Most lung carcinomas invaded the bronchial lumen or peripulmonary tissues.

- 0896 ARE THERE RENAL ADENOCARCINOMA-FREE POPULATIONS OF LEOPARD FROGS? (E.) McKinnell, R. G. (Dept. Zool., U. Minnesota, Minneapolis) and D. P. Duplantier. *Cancer Res* 30(11):2730-2735, 1970.

Two populations of leopard frog (*Rana pipiens*) were found to be free of renal adenocarcinomas and preliminary experiments in tumor promotion were performed on frogs from these groups. A group of 466 frogs collected in Louisiana were found to be tumor-free on autopsy; 2 of 12 frogs developed renal adenocarcinomas when injected in the embryo phase with cell-free extracts of a renal tumor. Of 980 frogs collected in North Dakota, 932 were autopsied and found to be tumor-free. Two renal adenocarcinomas developed in frogs from this group when they were kept at room temperature (20-22°) for 8 mo. It was suggested that the development of renal tumors in *Rana pipiens* is associated with pesticide use in agricultural areas.

- 0897 CARCINOGENICITY OF THE HERBICIDE MONURON. (Rus.) Rubenchik, B. L. (Sci. Res. Inst. Food Hyg., Kiev, U.S.S.R.), N. E. Botsman and G. P. Gorban. *Vop Onkol* 16(10):51-53, 1970.

The carcinogenicity of monuron herbicide [3-(p-chlorophenyl)-1,1-dimethylurea] was studied in 100 randombred white male rats, in 50 white randombred and 45 C57Bl male and female mice. The rats were given daily 450 mg/kg monuron in their diet for 18 months; the mice received 6 mg of monuron in milk p.o. once a wk for 15 wk. The total experimental period for rats lasted 27 months and 13 months for mice. The first tumor in rats appeared on the 18th wk of the experiment (microcellular lung cancer) in 1 rat; other cancers developed between 68-118 wk of experimentation. The first tumor in randombred mice appeared at 16 wk and after 4 wk in the C57Bl mice. Malignancy occurred in 15 rats, in 13 ran-

dombred and in 7 C57Bl mice; the liver and the lung appeared to be the main target organs. The malignant liver hepatomas exhibited a hepatocellular cancer structure with highly polymorphic cells, giant cells with hyperchromic nuclei, atypical mitoses and micronecroses. The lung tumors originated in the alveolar cells or in the bronchial epithelial lining, and the gastric tumors originated in the glandular epithelium. Tumor incidence was 46.5% in rats, and no tumors were found in controls. The incidence of both malignant and benign neoplasm was 56.5% in randombred, 26.9% in C57Bl mice, and 3.9% in C57Bl control mice.

- 0898 THE INDUCTION OF SARCOMA OF THE SKIN IN THE ALBINO RAT BY CADMIUM CHLORIDE. (Ger.) Knorre, D. (Dist. Hosp. St. Georg, Leipzig, Germany). *Arch Geschwulstforsch* 36(2):119-126, 1970.

Induction of a s.c. sarcoma by CdCl₂ (0.003 mM/100 g body wt, single dose) was studied in 80 male Wistar rats 12 wk-old at the beginning of the experiment. Spindle cell sarcoma developed at the injection site in 6 out of 45 surviving animals after 7-18 month latency periods. One rat sacrificed 248 days after injection exhibited disseminated peritoneal metastases; the other 5 rats had occasional regional lymph node metastases. No spontaneous skin or testicular tumors were noticed among the 20 control rats during the 23-month observation period.

- 0899 EFFECTS OF THE COADMINISTRATION OF THIAMINE ON THE INCIDENCE OF URINARY BLADDER CARCINOMAS IN RATS FED BRACKEN FERN. (E.) Pamukcu, A. M. (Coll. Vet. Med., U. Ankara, Turkey), S. Yalciner, J. M. Price and G. T. Bryan. *Cancer Res* 30(11):2671-2674, 1970.

The development of bladder and intestinal tumors in rats maintained on a diet containing bracken fern (*Pteris aquilina*) supplemented in some cases with thiamine was investigated. Male and female albino rats ingested daily a 25 g diet of about 1/3 bracken fern, or the same diet was given with thiamine (2 mg of thiamine hydrochloride weekly, s.c.). Most rats given either of the 2 test diets lived more than 6 months. Intestinal tumors were first detected in males and females on the experimental diets at the age of 6 months; bladder tumors were first detected in males and females at the ages of 9 and 7 months, resp. All of the rats that were given bracken fern alone or bracken fern and thiamine and survived more than 6 months developed intestinal tumors. Two of the 26 rats given bracken fern developed bladder tumors; 54 of the 90 rats given bracken fern and thiamine developed bladder tumors. Sixty nine percent of the females and 53% of the males in the bracken fern and thiamine group developed bladder tumors. The gross and microscopic morphological characteristics of bracken fern-induced tumors were identical to bladder tumors induced by the carcinogen N-[4-(5-nitro-2-furyl)-2-thiazolyl] formamide. No intestinal or bladder

ors developed in control rats receiving neither bracken fern nor thiamine. The increased incidence of bladder tumors in rats fed bracken fern and thiamine may have been due to an alteration of the absorption, distribution, metabolism, or excretion of the bracken fern carcinogen brought about by thiamine.

0 PROPERTIES OF THE SARCOMAS INDUCED BY FERRIDEXTRAN SPOFA IN INBRED RAT STRAIN AVN: THE OBSERVATION OF H-1^a AND B 1 ANTIGENITY OF FEDEX-AVN/3 TUMOR FOLLOWING LONG TERM *IN VITRO* CULTIVATION. (E.) Krenova, D. (Fac. Gen. Med., Charles U., Prague, Czechoslovakia), V. Kren and O. Krk. *Neoplasma* 17(5):505-512, 1970.

in vitro antigenicity of the FEDEX-AVN/3 tumor induced by Ferridextran Spofa) was analyzed by testing the H-1^a histocompatibility antigen and the thymocyte B 1 antigen by isoimmunization of allelic rat strains WP and LEW by tumor cells. Subsequent testing of the antisera was done against a panel of rat erythrocyte types, and the absorbency capacity of the tumor cells from *in vitro* cultivation was compared to that of syngeneic peritoneal cells). Both the H-1^a antigenic complex and B 1 erythrocyte antigen of the FEDEX-AVN/3 tumor were found to be fully preserved during the long term *in vitro* cultivation.

1 *IN VITRO* ASSAY OF THE STIMULATORY EFFECT OF BONE MARROW CELL PROLIFERATION OF SERA OBTAINED AFTER CHLORAMBUCIL TREATMENT. (E.) Niskanen, E. (2nd Dept. Path., U. Helsinki, Finland), T. Rönkä and E. Kivilaakso. *Acta Path Microbiol Scand* 78(5):589-594, 1970.

The effect of sera obtained from rats at various intervals (2, 5, 6, 8 and 9 days) after a single dose of chlorambucil (12 mg/kg, i.p.) on ³H-thymidine and ³H-adenine uptake in normal bone marrow cells was studied *in vitro*. ³H-Adenine incorporation (reflecting mainly the effect on RNA synthesis) by sera taken 9 days after treatment was increased by 29.2%. Sera taken after 5, 6, and 8 days increased the incorporation of ³H-thymidine by 19.1%, 20.3%, and 53.8%, resp.), while after 9 days only a slight stimulation (5.7%) was observed; these results paralleled the changes in the number of granulocytes found in the bone marrow (approximately 30% of the control value after 2 days and gradually rising to the control value by 9 days after chlorambucil treatment). Bone marrow cell proliferation may be due to the initial reduction of the number of cells.

2 FATE AND METABOLISM OF SOME MUTAGENIC ALKYLATING AGENTS IN THE MOUSE: I. ETHYL METHANESULFONATE AND METHYL METHANESULFONATE AT SUBLETHAL DOSE IN HYBRID MALES. (E.) Cumming, R. B. (Oak Ridge Natl. Lab., Tenn.) and M. F. Walton. *Int J Rad Biol* 10(4):365-377, 1970.

The metabolic fate of ethyl methanesulfonate (EMS, 0 mg/kg, i.p.) and methyl methanesulfonate (MMS,

150 mg/kg, i.p.) with a ¹⁴C-alkyl label (1 µC/g) in (101 x C3H)F₁ hybrid male mice was determined by measuring the radioactivity in various tissues, in the blood, urine, and exhaled ¹⁴C-carbon dioxide at various time periods ranging from 15 min to 24 hr after injection. Both EMS and MMS were rapidly distributed throughout the body, but MMS showed an uneven distribution (cpm/mg wet weight) with the tissues active in detoxification having higher levels of radioactivity (3200-13000) and peripheral tissues having lower levels (1200-2000). In circulating blood, EMS activities ranged from 200 at 15 min after injection to 650 at 4 hr after injection and MMS activity remained constant at 400-500 during the first 8 hr before declining. MMS-treated animals excreted 34% of the radioactivity in the urine during the first 24 hr while EMS-treated animals excreted only 15%; however, the EMS-treated animals excreted approximately 60% of the injected activity as ¹⁴C-carbon dioxide during the first 12.5 hr compared to 27% excreted by the MMS-treated animals.

0903 CHEMICAL MUTAGENESIS IN MAMMALS: THE CHINESE HAMSTER BONE MARROW AS AN *IN VIVO* TEST SYSTEM: HEMATOLOGICAL FINDINGS AFTER TREATMENT WITH TRENIMON. (Ger.) Boller, K. (U. Chil. Clin. Zurich, Switzerland) and W. Schmid. *Humangenetik* 11(1):35-54, 1970.

Trenimon-induced chromosomal damage was studied in the bone marrow of Chinese hamsters. The trenimon was given i.p. in saline in doses of 0.031-2 mg/kg. The bone marrow smears were taken from the femurs and analyzed qualitatively and quantitatively for Jolly bodies and leukocyte bodies; heart blood was used for hematological analysis. The quantitative changes in the bone marrow following trenimon administration were not conclusive. Qualitative changes revealed many pathological nuclear forms and a definite dose dependency. With high doses, cells with fragmented structureless nuclei were seen. The most striking changes appeared from 6-12 hr after 2 administrations in a 24-hr interval. If the percentage of pathological nuclei could be considered as a criterion of chromosome damage, this method offers a technique for toxicological screening of chromosome damaging agents and for mutagenicity testing.

0904 STUDIES IN RATS ON IMMUNOSUPPRESSIVE PROPERTIES OF CYTOSTATICS WITH SPECIAL CONSIDERATION OF CARCINOGENIC EFFECT. (Ger.) Scherf, H. R. (German Cancer Res. Inst., Heidelberg), C. Krüger and C. Karsten. *Arzneimittelforschung* 20(10):1467-1470, 1970.

The relationship between the immunosuppressive and the carcinogenic effects of the cytostatic compounds used in cancer chemotherapy was studied in Sprague-Dawley rats. Fifteen agents used in cancer therapy were tested by means of the hemagglutination test, the plaque test (according to Jerne), and quantitative immunodiffusion to discover their immunosuppressive action. The immune reaction following the single administration of a cytostatic drug (40% of the LD₅₀)

was manifested by a decrease in hemagglutinin titer only after methotrexate, 6-mercaptopurine, and endoxan. The immune reaction after the 7% of LD₅₀ injection once weekly over 14 wk, resulted in a decrease in the hemagglutinin titer in animals treated with 5-fluorouracil. Trenimon only decreased this titer after the first administration and then returned to normal. Results show that although the antimetabolites showed marked immunosuppressive properties, they do not appear to be carcinogenic. Other examples show that no correlation exists between the carcinogenic and immunosuppressive effects, under the conditions reported here.

- 0905 CANCEROGENIC ALKYLATING SUBSTANCES: IV. 1,3-PROPANE SULTONE AND 1,4-BUTANE SULTONE. (Ger.) Druckrey, H. (Max Planck Inst. Immunobiol., Freiburg, Germany), H. Kruse, R. Preussmann, S. Ivankovic, C. Landschütz and J. Gimmy. *Z Krebsforsch* 75(1):69-84, 1970.

Observations of local sarcomas following subcutaneous injection of dimethyl sulfate in rats led to the investigation of numerous alkylating substances for carcinogenic properties. When 1,3-propane sultone was tested in 12 rats by weekly s.c. injections of 30 or 15 mg/kg in 1% olive oil, local necroses appeared after several weeks; treatment was discontinued until these were healed. After 21 weeks and total doses of 390 or 210 mg/kg, histological examination revealed marked infiltration of the tumor into the cutaneous and muscular tissue, and one rat showed multiple pulmonary metastases. One animal, on the lower dose, developed an abdominal tumor; after a paraplegia of the hind quarters and a paralysis of the bladder, it was found at autopsy, that a neurogenic tumor developed in the lumbar area. The experiment was repeated with oral administration (8.5% of LD₅₀) by means of gavage, in 12 rats. In spite of the high activity of the 1,3-propane sultone and its rapid disturbance of the gastric function, a definite absorption could be demonstrated. The observation of 2 tumors in the cerebral region points to a certain neurotropy. I.V. administration of 1,3-propane sultone (40 mg/kg) weekly to 10 rats for 16 weeks resulted in the development of sarcomas in 3 animals with one mixed tumor in the brain of one animal. With a single i.v. injection, 9 of 32 animals treated with the carcinogen showed malignant tumors. The transplacental experiments yielded 7 tumors in 39 offspring after a single dose administered to the mothers. An analog, 1,4-butane sultone produced a markedly different reaction than 1,3-propane sultone in an acute experiment in rats. Administration by any route was followed immediately by a hypersensitivity that affected otherwise quiet animals with periodic jumping and stretch cramps; death resulted from clonic muscle twitching and spasms of the throat musculature. The results of s.c., i.v., or p.o. administration of 1,4-butane sultone, showed a carcinogenic effect less marked than that of propane sultone.

- 0906 EXPERIMENTAL STUDIES ON CARCINOGENIC EFFECTS OF ANTI-CANCER CHEMOTHERAPEUTICS AND IMMUNOSUPPRESSIVES. (Ger.) Schmähel, D. (German

Cancer Res. Ctr., Heidelberg) and H. Osswald. *Arzneimittelforschung* 20(10):1461-1467, 1970.

The carcinogenic action of the most important cancer chemotherapeutic agents was investigated. The study was carried out in 1284 male rats of the BR-46 line and 100 female mice of the NMRI-line; the male rats were more sensitive to the drugs tested than the female rats. The preparations tested were: alkylants, antimetabolites, naturally occurring compounds, peroxide forming compounds and antibiotics. To represent long term therapy, the animals were given 7% of the LD₅₀ (i.v. or by stomach tube) over 52 weeks, and for the short term study, the drugs were injected only 5 times at 2 week intervals. These animals died at a relatively young age compared to other carcinogen-treated animals, probably due to the frequent occurrence of infections. The carcinogenic effects of the alkylants (myleran, mitomen, endoxan, degranol, trenimon, thio-tepa) which were seen were different degrees of lymphatic and myelogenous leukemias, lymphosarcomas, pheochromocytomas, etc., in 11-30% of the treated animals. No carcinogenic effects were observed as a result of antimetabolite or natural product treatment. Of the antibiotics only sanamycin (actinomycin C) was tested in 22 rats and revealed 1 paramyeloblast leukemia and 1 intraabdominal carcinoma, 4 benign tumors and 3 thymomas and an adrenocortical adenoma. X-ray irradiation showed similar carcinogenic effects to those of alkylants. In the experiments for short term effects, vinblastine was found to be noncarcinogenic, whereas endoxan and mitomycin showed marked carcinogenic effects.

- 0907 NEOPLASMS OF URINARY BLADDERS OF HAMSTERS TREATED WITH 2-ACETYLAMINOFLUORENE AND INDOLE. (E.) Oyasu, R. (Northwestern U. Med. Sch., Chicago, Ill.), H. Sumie and H. E. Burg. *J Nat Cancer Inst* 45(5):853-860, 1970.

The induction of bladder tumors by injections of 2-acetylaminofluorene (AAF) together with dietary administration of indole was investigated in newborn male hamsters. Animals were given i.p. injections of AAF (5 mg/100 g body wt) 3 times/wk for 3 wk; at 3 wk of age, they were fed a synthetic diet containing 0.06% AAF and 1.6% indole. Of 26 hamsters surviving the experimental course, all developed transitional cell carcinoma in the bladder after 11 months; tumors were invasive in 24 cases. All animals showed diffuse or focal hyperplasia of the mucosa. Tumors often grew in multiple foci in the early stages, invading the basement membrane and the lamina propria. About 2/3 of the hamsters with bladder tumors had foci of acute and chronic inflammation. Although the livers of treated animals were often slightly decreased in size, no hepatomas were found. However, bile duct proliferation and fibrosis were present in varying degrees of severity. Other lesions less frequently observed included retroperitoneal histiocytoma, pancreatic adenocarcinoma, and papillary adenocarcinoma of the gallbladder.

- 0908 EFFECTS OF ADRENALECTOMY AND BILE DUCT LIGATION ON THE URINARY EXCRETION OF METABOLITES OF 2-ACETAMIDOFLUORENE BY MALE WEANLING RATS. (E.) Lotlikar, P. D. (Temple U. Sch. Med.,

Philadelphia, Pa.) and M. Gruenstein. *Biochem J* (5):921-923, 1970.

effects of bile-duct ligation and adrenalectomy on the urinary excretion of metabolites of the carcinogen 2-acetamidofluorene in rats were investigated. Male weanling rats were either adrenalectomized, subjected to bile-duct ligation or both, after which they were given an i.p. injection of 2-acetamidofluorene (3 mg/100 g body wt). Urine samples were then assayed for the presence of *N*-hydroxy-2-acetamidofluorene (*N*-hydroxy-AAF) and other metabolites of the carcinogen. Rats undergoing bile-duct ligation followed by 2-acetamidofluorene injection showed more than a 2-fold increase in excreted *N*-hydroxy-AAF compared to intact controls (controls, 1.55%; ligated animals, 2.03%). Excretion of 3-, 5-, and 7-hydroxy-AAF was also increased in bile duct-ligated rats. Bile-duct ligation of adrenalectomized rats resulted in a smaller increase in *N*-hydroxy-AAF excretion (2.03%). *N*-hydroxy-AAF excretion in the adrenalectomized and ligated group was decreased to about 58% of that in the ligated group.

9 REACTIVE PHOSPHATE ESTER OF THE CARCINOGEN 2-(*N*-HYDROXY)ACETAMIDOFLOURENE. (E.) Likar, P. D. (Temple U. Sch. Med., Philadelphia, Pa.) and M. B. Wasserman. *Biochem J* 120(3):661-665, 1970.

Interaction of *N*-acetoxyacetamidofluorene (*N*-acetoxy-AAF) with inorganic phosphate to form *N*-phosphate and ring phosphate esters is described. *N*-acetoxy-AAF was incubated with phosphate buffer at 25°C to give a water-soluble product with absorption peaks at 303, 290, and 280 nm, but *N*-hydroxy-AAF did not undergo this reaction. Methionine reacted with the phosphate-dependent polar fluorene derivative to give a product with the same R_f value (0.35-0.44) as synthetic 3-methylmercapto-AAF. The *N*-acetoxy-AAF phosphate derivative similarly reacted with guanosine to give a product with R_f value of 0.8-0.94, which probably was *N*-(guanosyl-8-yl)-AAF. *N*-acetoxy-AAF derivative was very labile and hydrolyzed by both acid and alkaline phosphatases with liberation of P_i and ether-soluble fluorene derivatives. These results suggested that the compound AAF-*N*-phosphate which may also decompose or rearrange to form an unreactive ring phosphate of AAF. It appears that AAF-*N*-phosphate might be formed *in vivo* by interaction of *N*-acetoxy-AAF and P_i or by enzymic conversion of *N*-hydroxy-AAF with ATP and P_i . This compound might be the ultimate carcinogenic metabolite of *N*-acetoxy-AAF, but attempts to detect phosphate metabolites of the parent compound in urine of rats treated with *N*-acetoxy-AAF were unsuccessful.

10 OVARIAN INFLUENCE ON PULMONARY CARCINOGENESIS BY HYDRAZINE SULFATE IN BALB/c/Cb/Se Mice. (E.) Biancifiiori, C. (Perugia U. Med. Sch., Italy). *J Nat Cancer Inst* 45(5):965-970, 1970.

Development of pulmonary carcinomas induced by hydrazine sulfate (HS) in gonadectomized mice,

and breeding mice, and intact virgin female mice was investigated. Mice in the various experimental groups were given daily doses of 1.13 mg HS by stomach tube beginning at 8 wk-of-age; 150 doses were given. Ninety percent of intact virgin mice developed pulmonary tumors; the average number of tumors developed by a mouse was 3. Breeders developed tumors in all cases, 14 tumors/mouse being the mean. Gonadectomized mice developed tumors in 60% of cases, and the average number of tumors/mouse was 5. The tumors developed by intact virgins and gonadectomized mice were most often adenomas (96%), with some carcinomas (3-4%). Breeders developed 47% carcinomas and 52% adenomas. No local spread or metastases were observed in tumors developed by gonadectomized mice, but both conditions occurred in 60% of breeders; there was metastasis to the adrenals in 2 mice. Liver tumors (hepatocarcinomas) were observed in 28% of the treated mice and ovarian tumors were observed in 24% of breeders. Apparently increased ovarian hormone production was associated with the greater biological and morphological malignancy of the tumors developed by breeding mice.

0911 THE DETERMINATION OF 3-HYDROXYANTHRANILIC ACID IN BLOOD SERUM IN THE EARLY STAGES OF EXPERIMENTAL CARCINOGENESIS. (Rus.) Korosteleva, T. A. (N. N. Petrov Sci. Res. Inst. Oncol., Leningrad, USSR) and A. T. Zasyпка. *Vop Onkol* 16(10):47-50, 1970.

A method for the immunological determination of 3-hydroxyanthranilic acid in animal sera during the early stages of benzidine carcinogenesis is presented. Five groups of C3HA mice (consisting of 10-15 animals each) and 5 groups of randombred rats (consisting of 5-7 animals each) were given benzidine (0.1 mg/g wt and 0.025 mg/g wt, resp.) in their daily diet for 4, 15, 30, 60 and 100 days. 3-Hydroxyanthranilic acid (3-HOAA) was determined as a serum haptene by means of an agar precipitin reaction against 3-HOAA antibody-containing rabbit sera obtained by i.p. immunization of rabbits with synthetic 3-HOAA azoproteins. A specific precipitin band in the experimental animal sera occurred after 4 (40% of mice and rats), 30 (30% of mice and rats) and 60 (in 50% of the animals) and 100 benzidine administrations (100% positivity); no such reaction was noticed in sera of animals treated 15 times and of control animals. The absence of the 3-HOAA-specific band in sera of the animals at the stage of 15 administrations may be due to an immunological removal of 3-HOAA or to compensatory mechanisms leading to a temporary recovery of tryptophan metabolism. Alterations in tryptophan metabolism seem to occur prior to or at the very early stages of carcinogenesis.

0912 DETECTION OF POLYCYCLIC AROMATIC HYDROCARBONS IN HUMAN CARCINOMATOUS TISSUE. (Ger.) Wagner, K. H. (Giessen Univ., Germany) I. Siddiqi and E. Wagner-Hering. *Naturwissenschaften* 57(11):547, 1970.

Tissue samples from human bronchial carcinoma were found to contain as much as 32 µg/100 g tissue of

3,4-benzpyrene, while samples from gastric carcinoma and rectal carcinoma contained 3,4-benzfluoranthene in amounts of 23 $\mu\text{g}/100\text{ g}$ and 13 $\mu\text{g}/100\text{ g}$ tissue, resp. Besides these compounds other unidentified fluorescent compounds were detected. These compounds seem to have accumulated in the gastrointestinal tract over a long time period via food ingestion. The presence of 3,4-benzfluoranthene in bronchial carcinoma tissues implicates its presence in the environmental air or in cigarette smoke. A certain critical level of polycyclic hydrocarbons apparently has to be accumulated prior to the beginning of the metastatic process.

- 0913 CARCINOGEN AND MICROSOMAL MEMBRANE INTER-ACTION: CHANGES IN MEMBRANE DENSITY AND ABILITY TO BIND NUCLEIC ACIDS. (E.) Kubinski, H. (U. Wisconsin Sch. Med., Madison) and C. B. Kasper. *Science* 171(3967):201-203, 1971.

The changes in the density of the nucleic acid-membrane complex formed through the binding of DNA (from *Escherichia coli*) or of synthetic copolymer polyribocytidylic-polyriboguanilyc acid (polyC-polyG) to microsomal membrane from rat liver were determined on cesium chloride gradients in the presence of various carcinogenic chemicals. Membrane incubated with polyC-polyG before centrifugation in cesium chloride peaked at a density of 1.18, while membrane incubated with DNA peaked at both 1.18 and 1.22. Incubation with 2-acetylaminofluorene (2 mg/ml) yielded DNA associated with a major peak at a density 1.22 and 2 minor peaks at 1.18 and 1.13, and polyC-polyG was associated with peaks at 1.15, 1.17, and 1.22. Incubation with N-acetoxy-2-acetylaminofluorene (2 mg/ml) yielded a DNA peak at 1.25 and a polyC-polyG peak at 1.19, while incubation with N-hydroxy-2-acetylaminofluorene (2 mg/ml) yielded complexes of densities between 1.19 and 1.25. With β -propiolactone (4mg/ml) a single peak was observed at 1.16, and with 3-methyl-1-p-tolyltriazine (2 mg/ml) a small peak was observed at 1.16 but most of the material was found at a higher density (1.18). Chemical carcinogens may act by interfering with the chemistry and biological activity of cellular membranes.

- 0914 AFLATOXIN B₁: CYTOTOXIC MODE OF ACTION EVALUATED BY MAMMALIAN CELL CULTURES. (E.)

Scaife, J. F. (Euratom Joint Res. Ctr., Ispra, Varese, Italy). *FEBS Letters* 12(3):143-147, 1971

The mode of action of aflatoxin B₁ was examined by observing the inhibition of RNA synthesis in various animal cells treated with aflatoxin B₁. Human kidney cells, HeLa S₃ cells, Chang liver cells, and 3T3 mouse cells were cultured in monolayers and exposed to aflatoxin B₁. The toxin rapidly inhibited RNA synthesis in rat liver cells, slices, or liver *in vivo*; after 1-3 hr of incubation of these tissues with aflatoxin, DNA synthesis was depressed to 44, 59, and 26% of control DNA synthesis rates, resp., in adult rat liver cells, liver slices, and liver *in vivo*. Inhibition of RNA synthesis in human kidney T cells, HeLa S₃ cells, and Chang liver

cells was more delayed. Ten $\mu\text{g}/\text{ml}$ of aflatoxin incubated with cells for 30 min gave 98 and 88%, resp., of control DNA synthesis for kidney T cells and Chang liver cells. Exposure of synchronized cell cultures to aflatoxin for up to 14 hr showed that the cells were retarded in passage through the S-phase, and that their DNA synthesis rates were decreased. Mitosis was also inhibited, apparently as a function of the amount of time cells exposed to aflatoxin took to complete the S-phase. Liver cells apparently converted aflatoxin B₁ to a more potent cytotoxin which was able to affect cells which were ordinarily not susceptible, a hypothesis which can explain the susceptibility of the liver to carcinogenesis induced by aflatoxin B₁.

- 0915 NUTRITION AND AFLATOXIN CARCINOGENESIS. (E.) Rogers, A. E. (Dept. Nutr. Food Sci., Massachusetts Inst. Technol., Cambridge) and P. M. Newberne. *Nature* 229(5279):62-63, 1970.

Interactions between nutritionally induced liver disease and carcinoma induced by aflatoxin were investigated. Diets marginal in lipotropes were associated with differences in the response of rats to aflatoxin. Male rats were maintained on a lipotrope-deficient diet or on a control diet; for acute toxicity studies rats were given a single i.p. dose of aflatoxin B₁ (7 mg/kg). The lipotrope deficiency protected all rats against doses of aflatoxin which were lethal to 60-100% of rats on the control diet. Rats on the lipotrope-deficient diet and a carcinogenic dose of aflatoxin B₁ (15 daily doses of 25 μg each) showed focal areas of hyperplastic abnormal hepatocytes which were thought to be preneoplastic. A close correlation was also observed between the early appearance of liver cell carcinomas and the lipotrope-deficient diet. Carcinomas had appeared in 25% of rats on the lipotrope-deficient diet 6 months after aflatoxin treatment, and in none of the rats on the normal diet at this point. The lipotrope-deficient diet decreased aminopyrine demethylase, *p*-nitroanisole demethylase, and benzpyrene hydroxylase activities relative to the values for these enzymes in rats on the control diet. The findings may indicate that aflatoxin B₁ is not itself toxic, but must be metabolized to a toxic product, a process which normally-nourished livers accomplish readily but which lipotrope-poor livers do not; the high tumor incidence in areas in which there is malnutrition and aflatoxin B₁ food contamination tend to support this hypothesis.

- 0916 EFFECTS OF AFLATOXIN ON SOME MARKER ENZYMES OF LYSOSOMES. (E.) Tung, H. T. (Dept. Poultry Sci., North Carolina St. U., Raleigh), W. E. Donaldson and P. B. Hamilton. *Biochem Biophys Acta* 222(3):665-667, 1970.

The effect of dietary aflatoxin on acid phosphatase and β -glucuronidase, 2 marker enzymes for lysosomes, was investigated in chickens. Male chicks were given graded doses of aflatoxin in their diet of commercial feed, and enzyme activity was assayed in sections of liver and breast muscle. Aflatoxin increased both enzyme activities, even at low doses.

phosphatase activity in muscle was 1.0 and $U \times 10^{-2}/mg$ protein, resp., at aflatoxin doses 0 and 2.5 $\mu g/g$. In liver, β -glucuronidase activity was at 1.0 and 2.4 $U \times 10^{-2}/mg$ protein, resp., at aflatoxin doses of 0 and 2.5 $\mu g/g$. Time courses of 48 hr were noticed between introduction of aflatoxin and the onset of significant increases in liver acid phosphatases, which were paralleled by increases in capillary fragility.

7 THE FORMATION OF AFLATOXINS B_{2a} AND G_{2a} AND THEIR DEGRADATION PRODUCTS DURING *IN VITRO* DETOXIFICATION OF AFLATOXIN BY LIVERS OF CERTAIN AVIAN AND MAMMALIAN SPECIES. (E.)

Person, D. S. P. (Central Vetr. Lab., Minist. of Agric., Fisheries, Food, Weybridge, Surrey, England) and B. A. Roberts. *Food Cosmet Toxicol* 8(5):527-538, 1970.

Aflatoxin G₁ was found to be metabolized as rapidly as aflatoxin B₁ in liver microsome preparations from chick, duckling, guinea pig and mice. Metabolic products of aflatoxins B₁ and G₁ included unidentified metabolites which were spectrally similar to the aflatoxin hemiacetals, B_{2a} and G_{2a}. Methanol extracts of liver incubations showed peak absorption at about 400 nm at pH 6.5 or greater, and the absorption was intensified when strong ammonia solution was added. The aflatoxin hemiacetals B_{2a} and G_{2a} were unstable in dilute phosphate-buffered protein solution (pH 7.4); in this reaction, the hemiacetals were first bound to protein, and then degraded to form yellow substances. Cysteine added in amounts of 5 mM inhibited the degradation of the aflatoxin hemiacetals; when cysteine was added to a standard incubation mixture, 50% of the aflatoxin was metabolized by chick liver fractions was spectrophotometrically identified as its hemiacetal. The toxicity of the aflatoxin hemiacetals may result from their instability in protein solutions.

8 EFFECT OF AFLATOXIN B₁ ON THE *IN VITRO* INCORPORATION OF ¹⁴C-ACETATE INTO HUMAN SKIN LIPIDS. (E.) Black, H. S. (VA Hosp., Houston, Texas), J. D. Smith, B. J. Austin, and E. W. Schkolb. *Experientia* 26(12):1292-1293, 1970.

The effect of aflatoxin B₁ on the incorporation of ¹⁴C-labeled acetate into human skin lipids was investigated *in vitro*. Fresh human skin preparations were made from male Caucasians, and treated with $1 \mu g$ aflatoxin B₁ and $1 \mu C$ of ¹⁴C-acetate. Aflatoxin B₁ inhibited the incorporation of labeled acetate into the total lipid, phospholipid, free sterol, and neutral fat fractions of human skin. Total lipid incorporation of ¹⁴C-acetate in aflatoxin-treated preparations was at 23.55 cpm $\times 10^{-3}/100 mg$ protein wt, as compared to 40.02 cpm $\times 10^{-3}/100 mg$ for untreated control preparations. Phospholipid incorporation of labeled acetate decreased from 3.69 $\times 10^{-3}/\mu g P_i$ in controls to 2.49 cpm in aflatoxin-treated preparations.

19 EFFECT OF PHENOBARBITAL PRETREATMENT ON THE ABILITY OF AFLATOXIN B₁ TO INHIBIT

RIBONUCLEIC ACID SYNTHESIS IN RAT LIVER. (E.) Gumbmann, M. R. (Western Reg. Res. Lab., Albany, Calif.) and S. N. Williams. *Biochem Pharmacol* 19(11):2861-2866, 1970.

The effect of pretreatment with phenobarbital on nucleic acid synthesis inhibition by aflatoxin B₁ in rat liver was investigated. Male rats were given daily i.p. injections of sodium phenobarbital (75 mg/kg) for 5 days; shortly before death, rats were given a single i.p. injection of aflatoxin B₁ (1.5 mg/kg). Either phenobarbital or aflatoxin was withheld in controls. Without phenobarbital, a 28.3% reduction in nuclear RNA synthesis was seen in 4.5 hr in aflatoxin-treated rats, while with phenobarbital the nuclear RNA reduction was 8.6%. Cellular RNA/DNA ratios in aflatoxin-treated rats were decreased by 4%, while in rats pretreated with phenobarbital, the reduction of nuclear RNA/DNA was 3.1%. The inhibition of the uptake of ¹⁴C-labeled orotic acid by nuclear RNA by aflatoxin was 65.1%, but only 36.5% in rats pretreated with phenobarbital. Phenobarbital treatment alone produced a marked increase in liver wt in rats without changing the DNA level, suggesting that liver growth resulted primarily from cellular enlargement as opposed to cellular proliferation.

0920 BIOCHEMICAL CHANGES IN LIVER DUE TO AFLATOXIN. (E.) Shankaran, P. (Vallabh-bhai Patel Chest Inst., U. Delhi, India), R. Shankaran, H. G. Raj and T. A. Venkatasubramanian. *Brit J Exp Path* 51(5):487-491, 1970.

The effect of aflatoxin treatment on lipid content, glycogen content, protein content and enzyme activity in the liver was investigated in mice. Male mice were given i.p. injections of aflatoxin B₁ at a dose of 1 mg/kg body wt, and assays were performed 2 and 8 hr later. No change was observed in the liver content of glycogen, lipid or protein in treated mice 2 hr after injection of aflatoxin. Significant decreases were found in the activities of aconitase, malate dehydrogenase in the supernatant fraction of liver preparations and ATPase; significant increases were found in isocitrate dehydrogenase, fumarase, and malate dehydrogenase activity in the particulate fraction. Eight hr after injection with aflatoxin, aconitase activity was recorded as 107 U/mg protein in treated mice and 160 U/mg in controls; similar figures for malate dehydrogenase were 337 U/g protein for aflatoxin-treated mice and 376 U/g protein for controls. Fumarase activity in control mice after 8 hr was recorded as 5525 U/g protein and 3282 U/g for controls; isocitrate dehydrogenase activity in controls was 24 U/g after 8 hr and in ATPase treated mice, 31.9 U/g. In the case of aconitase, fumarase and ATPase, changes obtained 8 hr after aflatoxin treatment were the opposite of those obtained 2 hr after treatment. Mitochondrial injury by aflatoxin and altered protein synthesis may account for these results.

0921 BINDING OF DIMETHYLAMINOAZOBENZENE METABOLITES TO DNA AND PROTEINS: I. *IN VITRO*

STUDIES ON A MICROSOMAL DEPENDENT SYSTEM. (E.)

Meunier, M. (Inst. Res. Sci. Cancer, Villejuif, France) and J. Chauveau. *Int J Cancer* 6(3):463-469, 1970.

The binding of dimethylaminoazobenzene (DAB) metabolites to DNA and proteins was investigated *in vitro*. DAB (aniline ring- $U^{14}C$) was incubated with NADPH, purified thymus DNA and rat liver microsomes. In this system, DAB that was bound to DNA measured 41.3 μ moles DAB/g DNA; DAB bound to microsomal proteins measured 453 μ moles DAB/g protein. When microsomes were omitted from the incubation system, or replaced by boiled microsomes or by enzymatically inactive protein, DNA labeling was drastically reduced (2.1 μ moles DAB/g DNA for a microsome free system). This finding appeared to indicate that a metabolic activation was required for binding to occur. NADPH was necessary for binding of DAB, for in systems in which NADPH was left out, bound DAB measured 0.7 μ moles/g DNA and 10 μ moles/g protein. Doubling the amount of microsomes in the incubation medium approximately doubled the binding of DAB to DNA. The amount of DAB metabolites increased with time of incubation, the increase being linear for the first 15 min, then dropping off for the next 30 min. Binding of DAB also depended on the pH of the medium; an 8-fold increase in binding was found when the pH was 7.4 compared to the value found with pH 6 (41 and 5 μ moles bound metabolites of DAB/g DNA, resp.). These findings suggested that the process of activation of DAB binding was enzymatic in nature. The kinetics of the binding of DAB metabolites to proteins were similar to the kinetics of the binding of DAB metabolites to DNA. After treatment of rats with 3-methylcholanthrene for 2 days, there was a 10-fold increase in the DNA binding and a 6-fold increase in protein binding, compared to control rat microsomes. Binding of DAB metabolites to DNA and protein was thought to be of a covalent nature.

0922 ENZYMIC ACTIVITY AND MORPHOLOGICAL ALTERATIONS IN LIVERS OF RATS FED ON *p*-DAB (DIMETHYLAMINOAZOBENZENE). (E.) Cerny, E. (Med. Fac., J. E. Purkyne U., Brno, Czechoslovakia) and F. Papousek. *Scripta Med* 43(3-4):143-150, 1970.

The effect of *p*-dimethylaminoazobenzene (DAB) treatment on liver enzyme activity and morphology was investigated in rats. Livers of rats fed 0.06% DAB in the diet showed increasing dystrophic alterations progressing in time to oligocellular necrosis, an increase in lymphocytes, increasing cholangiolar hyperplasia, and deposition of iron pigment in Kupfer cells. One cholangiocarcinoma and 2 adenomas were observed. Acid phosphatase activity was increased in the treated animals (17-49%) compared to untreated controls (14%). Nonspecific esterase with alpha-naphthylacetate activity was generally higher in treated rats than in controls, normal values being 16% and experimental values ranging from less than 16% in 3 of 50 cases to a maximum of 46%. Nonspecific esterase with naphthol AS-acetate activity was higher in treated rats than in controls. Succinic acid de-

hydrogenase activity was also higher in treated rats than in controls, mean values for controls being 3.8% and values for treated animals exceeding this level in 49 of the 50 cases, with an experimental maximum of 10.8%.

0923 AZO-DYE BINDING TO PROTEINS AND DETOXICATION OF *p*-DIMETHYLAMINOAZOBENZENE IN MOUSE AND HAMSTER LIVER. (E.) Decloitre, F. (Inst. Res. Sci. Cancer, Villejuif, France) and M. Meunier. *Int J Cancer* 6(1):481-487, 1970.

Protein-bound azodyes, azoreductase, and NADPH-cytochrome *c* reductase in the livers of rodents maintained on a regimen of *p*-dimethylaminoazobenzene (DAB) were investigated. Male mice of the IC and C3H strains and male hamsters were fed DAB (60 mg/kg body wt) in their diets. IC mice showed no histological abnormalities in their livers until 6 months after the start of DAB feeding, at which time glycogen and fat deposits together with an inflammatory reaction were seen. These abnormalities were noted in C3H mice 6 wk after the beginning of DAB feeding. By the third month livers of C3H mice showed nodules of increasing size and density, progressing to carcinoma in some cases. One yr after the beginning of DAB feeding hamster livers showed little or no abnormal effects. C3H mice exhibited azodye binding to proteins far in excess of that shown by IC mice or hamsters. Three wk after the beginning of treatment, C3H mice showed azodye binding at a maximum level of 18 μ mole bound azodye/100 mg protein. Three-wk azodye binding values for IC mice and hamsters were 5 and 2.5 μ moles, resp. Proteins from hamsters and IC mice were bound to azodyes at comparable levels throughout the course of the experiment. Azoreductase activity was 5 times greater in control IC mice than in C3H mice; in hamsters, activity was intermediate. The 3 kinds of control animals had similar NADPH-cytochrome *c* reductase activity. Both azoreductase and NADPH-cytochrome *c* reductase increased with DAB feeding in IC mice; increases were 60% at 1 wk and 40% at 2 wk of DAB feeding. DAB feeding decreased azoreductase after 3-6 months in C3H mice, while NADPH-cytochrome *c* reductase was increased by 65% in this strain. DAB had no marked effect on enzyme levels in hamsters. The sensitivity of C3H mice to DAB toxicity might be related to their low levels of azoreductase activity, while high azoreductase activity in IC mice probably allows adequate detoxication of DAB to prevent its toxic effects.

0924 CARCINOGENIC ACTIVITY OF DIBENZOTHIOPHENE: ANALOGS OF *p*-DIMETHYLAMINOAZOBENZENE. (E.) Brown, E. V. (Dept. Chem., U. Kentucky, Lexington) and R. Isbrandt. *J Med Chem* 14(1):84-85, 1970.

Four isomers of *p*-dimethylaminophenylazodibenzothiophene were prepared and tested for carcinogenicity in the rat liver. While *p*-dimethylaminoazobenzene in 0.06% concentrations produced hepatocarcinomas in 7 of 10 rats at 4 months and in 9 of 10 rats at 6 months, the 4 isomers of *p*-dimethylaminophenylazodibenzothiophene produced no tumors when tested at the same concentrations for 6 months.

5 ADRENOCORTICAL LIPID HYPERPLASIA INDUCED IN RATS BY ANILINE: A HISTOLOGIC AND ELECTRON MICROSCOPIC STUDY. (E.) Kovacs, K. (Inst. Exp. Surg., U. Montreal, Quebec, Canada), J. Blascheck, E. Yeghiayan, S. Hatakeyama and C. Dell. *Amer J Path* 62(1):17-34, 1971.

adrenal cortex of rats injected with aniline (5 mg, s.c.) was subjected to electron microscopic studies. Seven to 14 days after injection of aniline, adrenals were enlarged, and the cortices were markedly broader. Changes in the adrenals of treated rats were more pronounced in the inner cortical layers than in the zona glomerulosa. The numbers of lysosomes in aniline treated rats were increased, and the mitochondrial matrices were more conspicuous and showed swelling and rarefaction. Mitochondrial protrusions were noted in some mitochondria. Abundant lipid droplets were found in both treated and untreated adrenals; no marked changes were observed in the vasculature, nuclei, Golgi complexes, collagen particles, or free ribosomes of aniline-treated rats. The most striking change was seen in the adrenal cortex of rats given aniline for 7 or 14 days; extensive accumulation of lipid droplets occurred in the cytoplasm. In some cells lipid droplets coalesced and enlarged to the extent that they occupied the whole cytoplasm, masking the nuclei and distending the cells. Long, rectangular or needle-like crystals were seen in the cytoplasm of some treated cells. More variation in shape and size of mitochondria, enlargement of the endoplasmic reticulum and prominent Golgi apparatus were seen in the adrenals after 7 or 14 days of aniline treatment. In general, the alterations observed in adrenals of rats treated with aniline resembled those seen in certain types of congenital human adrenal hyperplasia. Aniline may inhibit cellular steroidogenesis, leading to decreased hormone secretion and perhaps adrenal enlargement.

6 BIOLOGICAL EFFECTS OF 7,12-DIMETHYLBENZ(a)ANTHRACENE (DMBA). ABSORPTION OF DMBA AT GASTROINTESTINAL LEVEL IN MICE. (Fr.) Gentil, J. (Inst. Res. Sci. Cancer, Villejuif, France), C. L. and I. Chouroulinkov. *Bull Cancer* 57(2):269-274, 1970.

The distribution of 7,12-dimethylbenz(a)anthracene (DMBA) at the gastrointestinal tract levels was investigated in ICI mice after p.o. and i.v. administration of the tritium-labeled compound. DMBA-³H dissolved in olive oil was given p.o. (0.6 ml containing 100 µC per mouse) to 2 groups of mice on an empty stomach; one group consisted of pretreated mice which had been receiving unlabeled DMBA (1 mg p.o. daily) for 4 months, and the second group consisted of untreated mice. Another group of mice pretreated with DMBA and untreated) were administered a suspension of DMBA-³H in colloidal aqueous solution (0.5 ml containing 100 µC) in the caudal vein. The mice were sacrificed 6, 15, 18, 24, 48 and 72 hr after the treatment. A 10-20-fold higher label accumulation in the cardiac stomach region with respect to the other organs of the gastrointestinal tract was noticed in both pretreated

and normal mice 1 hr following oral administration of the hydrocarbon. High levels of label were also noticed in the small intestine 6 hr and in the mesentery 15-19 hr after oral treatment in the pretreated mice, which were similar to the levels found throughout the other segments of the intestinal tract in the latter. I.V. administered DMBA-³H led to the appearance of homogeneous radioactivity within both the glandular and cardiac stomach, small intestine and mesentery with no appreciable differences between pretreated and untreated animals. The largest amounts of DMBA were bound by the liver and kidney which are the main routes of its excretion after i.v. administration. A correlation between the difficulty of induction of cancer in the glandular stomach by p.o. DMBA administration and its transportability through cell membranes at this level was confirmed. The changes observed at the mesenteric level in pretreated mice following p.o. DMBA-³H administration confirmed the hypothesis that DMBA induces mesenteric tumors.

0927 EFFECTS OF PROLACTIN OR GROWTH HORMONE ON GROWTH OF CARCINOGEN-INDUCED MAMMARY TUMORS OF ADRENO-OVARIETOMIZED RATS. (E.) Nagasawa, H. (Nat'l. Cancer Ctr. Res. Inst., Tokyo, Japan) and R. Yanai. *Int J Cancer* 6(3):488-495, 1970.

The effect of prolactin and bovine growth hormone (GH) on the growth of 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary tumors was investigated. Immature female rats were given i.v. injections of 5 mg of DMBA, and when palpable mammary tumors had developed, rats were adreno-ovariectomized. Adreno-ovariectomized animals were injected twice daily i.v. with GH (1.5 mg) or prolactin (1.25 or 2.5 mg). Prior to hormone injection, there was little difference in the body wt of the rats; however, adreno-ovariectomized rats treated with GH showed a 23% increase in body wt, while those treated with 2.5 mg prolactin showed an 18% decrease. The number of tumors which developed in intact controls, adreno-ovariectomized and prolactin-treated (1.25 mg prolactin), and adreno-ovariectomized and prolactin-treated (2.5 mg prolactin) rats increased by 33, 124 and 239%, resp. The number of tumors which developed in adreno-ovariectomized controls and in adreno-ovariectomized and GH-treated rats decreased gradually. Prolactin treatment in both doses increased the size of mammary tumors markedly; tumors occurring in rats given 2.5 mg of prolactin continued to increase in size after the growth of tumors developed by rats given 1.25 mg prolactin had leveled off. GH had no effect on tumor growth; however, it accelerated the growth of normal mammary glands. Administration of 2.5 mg prolactin beginning 20 days after adreno-ovariectomy increased the number and size of regressed mammary tumors to pre-operative levels, but the 1.25 mg dose had no effect. Apparently, prolactin is the hormone mainly responsible for the growth of tumors induced by DMBA.

0928 FURTHER STUDIES OF THE EFFECT OF BONE MARROW CELLS ON CHEMICALLY INDUCED

LYMPHOMA IN C57BL/6 MICE. (E.) Chen, L. (Weizmann Inst. Sci., Rehovoth, Israel). *Brit J Cancer* 24(3): 554-560, 1970.

The effect of syngeneic bone marrow cell inoculation on chemically induced lymphoma was investigated in C57BL/6 mice. Young mice were given intragastric doses of 7,12-dimethylbenz(a)anthracene (DMBA) followed by 15×10^6 syngeneic bone marrow cells; other groups of mice were exposed to whole body X-irradiation (170 rads) followed by syngeneic bone marrow cells. DMBA treatment alone induced lymphomas in 52% of mice, while DMBA plus bone marrow cells induced lymphomas in 45% of cases. X-irradiation alone effected a 77% incidence of tumors, while irradiated mice which were given bone marrow cells or bone marrow cells plus DMBA developed lymphomas in 28 and 33% of the cases, resp. The thymus glands of mice treated as described were weighed in order to test the regenerative effect of bone marrow cells on the DMBA-injured thymus; it appeared that bone marrow cells did not hasten thymic regeneration. Bone marrow cells from DMBA-treated and untreated mice were tested for their ability to prevent radiation leukemogenesis, with the result that lymphoma development was prevented in 33% of mice given marrow cells from treated mice and 28% of mice given marrow cells from untreated mice. Bone marrow cells from DMBA-treated mice were no more effective than bone marrow cells from untreated mice in repairing radiation damage to the thymus, or in preventing the lethal action of high doses of irradiation. Neither did marrow cells succeed in restoring antibody formation to Shigella which was depressed by DMBA. Apparently, bone marrow cells inhibit a specific stage in radiation leukemogenesis, but are not involved with the leukemia process as such.

0929 EFFECTS OF RESERPINE ON DEVELOPMENT OF 7,12-DIMETHYLBENZANTHRACENE INDUCED MAMMARY TUMORS IN FEMALE RATS. (E.) Welsch, C. W. (Dept. Anat., Michigan St. U., East Lansing) and J. Meites. *Experientia* 26(10):1133-1134, 1970.

The effect of reserpine, reportedly an enhancer of mammary development, on mammary tumors induced by 7,12-dimethylbenz(a)anthracene (DMBA) was studied in immature female rats. Rats were given doses of either 10 μ g or 100 μ g reserpine/100 g body wt (s.c. injections) followed by a single i.v. injection of 5 mg DMBA. Another group was treated with reserpine in comparable amounts after the appearance of DMBA-induced mammary tumors. Reserpine treatment at 100 μ g doses reduced the incidence of DMBA-induced mammary tumors, with rats given 0 or 10 μ g reserpine developing tumors in 100% of cases and rats given 100 μ g reserpine developing tumors in 81% of cases. Average numbers of tumors/rat were decreased by reserpine treatment, averages for control, 10 μ g-treated, and 100 μ g-treated animals being 10.9, 7.5 and 3.3, resp. The wt of induced tumors was also lower in reserpine-treated rats. Mean latency of tumor development was similar in control rats and rats given 10 μ g reserpine (68-70 days); however, 100 μ g doses of reserpine increased

mean latency to 98 days. Growth and development of mammary tumors was significantly increased by treatment with 10 μ g of reserpine after onset of tumor development. However, reserpine failed significantly to affect tumor development in ovariectomized female rats.

0930 GROWTH INHIBITION OF RAT MAMMARY CARCINOMA AND ENDOCRINE CHANGES PRODUCED BY 2-Br- α -ERGOCRYPTINE, A SUPPRESSOR OF LACTATION AND NIDATION. (E.) Heuson, J. C. (J. Bordet Inst., Brussels, Belgium), C. Waelbroeck-Van Gaver and N. Legros. *Europ J Cancer* 6(5):353-356, 1970.

The effect of injecting 2-Br- α -ergocryptine (CB-154) into rats bearing tumors induced by 7,12-dimethylbenz(a)anthracene was investigated. Female rats were administered the carcinogen at 50 days of age; when mammary carcinomas had developed, they were administered s.c. injections of CB-154 daily in doses of 3 mg/kg for 3 wk. In the CB-154-treated group of rats, 18 of 27 tumors decreased in size while 9 tumors increased or remained unchanged; in this group only 16 new tumors developed. In the untreated control group, 8 tumors decreased in size, 19 increased or remained unchanged, and 32 tumors were newly formed. CB-154 also produced accumulation of a large number of corpora lutea and shortened the estrus cycle; the corpora lutea seemed inactive with respect to the secretion of progestational compounds and did not undergo normal involution. Interference of CB-154 with prolactin secretion is probably responsible for the effect of the drug on tumor growth and on endocrine functions.

0931 REPLICATION OF DNA AFTER BINDING OF THE CARCINOGEN 7,12-DIMETHYLBENZ[a]ANTHRACENE. (E.) Bates, R. R. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), S. D. A. Eaton, D. L. Morgan and S. H. Yuspa. *J Nat Cancer Inst* 45(6):1223-1228, 1970.

This study was designed to determine the ability of DNA in cell cultures of mouse skin to replicate after binding of 7,12-dimethylbenz(a)anthracene- 3 H (3 H-DMBA). Full thickness skin from term fetuses of mice of the NIH General Purpose Swiss strain was dissociated with 0.5% trypsin followed by exposure to pancreatic deoxyribonuclease I. After growth and reseeded, cells were incubated in medium containing 7,12-dimethylbenz(a)anthracene- 3 H and thymine-free medium containing 5-bromodeoxyuridine in varying sequence. After suitable exposure to the media, DNA was extracted, fractionated by gradient centrifugation and absorption measured at 260 nm; half as much DMBA was bound to DNA which had replicated after removal of DMBA from the culture medium as was bound to the DNA which had not replicated during this period. Replication of carcinogen-bound DNA may lead to altered base-pairing, giving rise to inherited mutation although repair mechanisms can allow for generation of normal cells.

0932 SUPPRESSION OF CARCINOGEN-INDUCED RAT MAMMARY TUMOR FORMATION BY ACTINOMYCIN D.

Anderson, K. M., (Dept. Path. Chem., U. Toronto, Toronto, Ontario, Canada) and J. A. Kellen. *Experientia* 26(9):1000-1001, 1970.

Effect of actinomycin D on tumorigenesis induced by 7,12-dimethylbenz(a)anthracene was investigated in rats. Rats were injected with 7,12-dimethylbenzanthracene (DMBA) and 25 µg of actinomycin D, the injection of the latter agent either preceding or following the injection of DMBA by 20 min. Rats given the carcinogen alone developed palpable mammary tumors in 100% of cases from 50-200 days after treatment, while 25% of the rats given carcinogen followed by actinomycin D developed tumors, and 28% of the rats given actinomycin D prior to carcinogen administration developed tumors. Rats given carcinogen followed 1 min later by actinomycin D developed tumors in 22% of cases. No apparent effect on the estrous cycle of treated rats was observed, which indicates that neither the pituitary, the testes, nor the ovaries are affected by actinomycin D.

3 STRUCTURE AND ACTIVITY IN CHEMICAL CARCINOGENESIS: REACTIVITY AND CARCINOGENICITY OF 7-BROMOMETHYLBENZ[a]ANTHRACENE AND 7-METHYLBENZ-12-METHYLBENZ[a]ANTHRACENE. (E.) Dipple, (Roy. Cancer Hosp., London, England) and T. A. De. *Europ J Cancer* 6(5):417-423, 1970.

Comparison of the carcinogenic activities of two 7-methylbenz(a)anthracenes with those of their parent hydrocarbons in groups of 10 CB-Hooded adult male rats is reported. Under the conditions of the test (25 µg s.c.), the cumulative number of rats with sarcoma at the injection site using 7-methylbenz(a)anthracene was 1 at 6 months, 2 at 9 months, 2 at 12 months; using 7,12-dimethylbenz(a)anthracene tumor incidence was 8 at 6 months, 9 at 9 months and 9 at 12 months; with 7-bromomethyl-12-methylbenz(a)anthracene 6 tumors were found at 6 months, 9 at 9 months, and 10 at 12 months. The carcinogenicity of 7-bromomethyl-12-methylbenz(a)anthracene was comparable to its parent, 7,12-dimethylbenz(a)anthracene and considerably greater than its hydrolysis product, 7-hydroxymethyl-12-methylbenz(a)anthracene; 7-bromomethylbenz(a)anthracene was less active than its parent, 7-methylbenzanthracene. A direct relationship appeared to exist between chemical reactivity and carcinogenic potential.

4 THE BINDING OF BENZ[a]ANTHRACENE TO REPLICATING AND NONREPLICATING DNA IN CELL CULTURE. (E.) Yuspa, S. H. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.) and R. R. Bates. *Proc Soc Exp Biol Med* 135(3):732-734, 1970.

The binding capacity of ³H-benz(a)anthracene (BA) was tested in fetal mouse skin cell cultures utilizing 5-bromodeoxyuridine, and the replicating DNA was separated from non-replicating DNA after 20 hr incubation by density gradient ultracentrifugation. ³H-BA was found to be bound to both newly synthesized DNA (at which incorporated 5-bromodeoxyuridine) and to

non-replicating DNA, which indicated that synthesis is not a requirement for binding. However, BA, a weak carcinogen, was found to bind very poorly to DNA compared to 7,12-dimethylbenz(a)anthracene, a strong carcinogen.

0935 THE POSSIBLE ROLE OF RIBOFLAVIN DEFICIENCY IN EPITHELIAL NEOPLASIA: II. EFFECT ON SKIN TUMOR DEVELOPMENT. (E.) Wynder, E. L. (Sloan-Kettering Inst. Cancer Res., New York, N.Y.) and P. C. Chan. *Cancer* 26(6):1221-1224, 1970.

The effect of riboflavin deficiency on the development of epithelial neoplasms was investigated in mice. Female mice were fed a vitamin B₂-deficient diet for a wk, then returned to a normal diet shortly before being given a topical dose of 75 µg of 7,12-dimethylbenz(a)anthracene (DMBA). Vitamin-deficient mice developed tumors in greater numbers than normally-fed controls given DMBA; by 17 wk after DMBA treatment, control mice had developed tumors in 55% of cases, while mice given DMBA from 7 days before the reinstitution of the normal diet to 2 days after the recovery from riboflavin deficiency had developed tumors in 80-90% of cases. All tumors were papillomas. Mice given DMBA 7 days before recovery from vitamin deficiency developed an average 4.7 tumors/mouse, while mice in other vitamin-deficient groups developed 3.0-3.5 tumors/mouse, and controls developed an average of 1.6 tumors/mouse. Accelerated tumor development occurred in mice given DMBA after 5 wk of deficient diet and then painted with 1% croton oil twice weekly after being put back on a normal diet. In mice fed a normal diet injected with riboflavin before DMBA treatment the tumor yield did not differ from that of the controls, suggesting that riboflavin treatment itself does not counteract the initiating effect of DMBA, nor the tumor-promoting effect of croton oil.

0936 ELIMINATION AND METABOLISM OF BENZO(a)-PYRENE AFTER INTRATRACHEAL INJECTION. (Ger.) Dehnen, W. (Med. Inst. Air Pollut. Silicose Res., U. Düsseldorf, Germany), R. Tomingas, E. G. Beck, N. Manojlovic and M. Kirch. *Z Krebsforsch* 75(1):14-22, 1970.

Benzo(a)pyrene (BP) elimination from the lung through the blood stream following intratracheal injection was studied in Wistar rats. BP determinations were made by perfusion of the lung for 1 hr with saline and compared to untreated rat lungs in which recovery studies had been done with 5-16 µg of BP. The metabolic degradation of BP was studied in treated and untreated rat lung homogenates, lung microsomal fractions, liver microsomal fractions and in *in vitro* guinea pig alveolar and peritoneal macrophage cultures. Approximately 2-5% of the added BP (5-16 µg) was recovered with perfusion within 1 hr from the lungs of the untreated rats. The treated rats had 200 µg of BP in the lung 24 hr after intratracheal administration, and 1% was eluted following 1 hr of saline perfusion. The blood levels of BP following intratracheal adminis-

tration of 200 μg were 0.2 μg /total blood volume (considered to be 50 ml/1000 g body wt) 1 hr following administration and reached a peak value of 0.55 μg at 3 hr; then it returned to 0.2 μg 72 hr after intratracheal injection; when BP was given p.o. (100 μg and 1000 μg) the blood levels of BP were 0.033 and 0.035, resp. Lung homogenate and microsomal fractions from intracheally treated animals prepared 2.5 hr after BP administration and incubated with 2 μg of BP degraded 0.009 μg /mg protein and 0.025 μg /mg protein, resp; liver microsomes metabolized 0.3 μg /mg protein. Alveolar macrophage cultures incubated with BP and examined by fluorescence microscopy revealed a diffuse intracytoplasmic distribution of BP. The metabolism of 2.87×10^{-3} μg BP by 10^6 cells within 20 hr indicated the extent of the metabolizing capacity of guinea pig alveolar macrophages. The elimination of the inhaled BP from the lung appears to depend mainly on the functional condition of the alveolar macrophages.

- 0937 COMPARATIVE STUDIES ON THE INTERACTION OF BENZO[a]PYRENE WITH CELLS DERIVED FROM POIKILOthermic AND HOMEOTHERMIC VERTEBRATES: I. METABOLISM OF BENZO[a]PYRENE. (E.) Diamond, L. (Wistar Inst. Anat. Biol., Philadelphia, Pa.) and H. F. Clark. *J Nat Cancer Inst* 45(5):1005-1011, 1970.

The capacity to metabolize the carcinogen benzo(a)pyrene (BP) and the cytotoxicity of BP were investigated in warm- and cold-blooded organisms, including birds, rodents, reptiles, amphibians and fish. Monolayer tissue cultures from these organisms were inoculated with ^3H -BP, and after 24 hr of incubation with the carcinogen the amount of BP metabolized/cell was calculated from the ^3H -BP equivalents in the aqueous phase of a chloroform:methanol:water extraction mixture. Mouse embryo and hamster embryo cells were highly efficient in the metabolism of BP, showing values of 0.51 and 1.12 μg ^3H -BP degraded/ 10^7 cells/24 hr, resp. Other highly efficient cells were box turtle heart cells (1.30 μg), tokay gecko lung (1.41 μg), and American toad embryo (2.42 μg). Cells which metabolized from 0.25-0.50 μg ^3H -BP/ 10^7 cells/24 hr included bluegill fry, leopard frog embryo, and green iguana liver. Cell cultures metabolizing less than 0.25 μg of ^3H -BP included chick embryo, Russell's viper spleen and lung, and side-necked turtle heart. The most efficient metabolizer of BP was American toad embryo (2.42 μg). BP showed cytotoxicity only in cell cultures which were highly efficient metabolizers of the carcinogen.

- 0938 ISOLATION OF A BENZ[a]PYRENE-THYMINE PHOTOADDUCT FROM DNA HYDROLYZED AFTER IRRADIATION AT 365 nm IN THE PRESENCE OF BENZ[a]PYRENE. (E.) Antonello, C. (Inst. Chem. Pharm., U. Padua, Italy) and F. Carlassare. *Z Naturforsch* 256(11):1269-1271, 1970.

The products of the photoreaction between benzo(a)pyrene and DNA (from salmon sperm) which occurs af-

ter irradiation at 365 nm were isolated by precipitation and hydrolysis of the macromolecule followed by column (alumina) and thin layer (cellulose powder MN 300) chromatography. Four fluorescent substances with almost identical UV absorption spectra were separated on the chromatoplates with R_f values (distance of substance from origin/distance of benzo(a)pyrene from origin) of 2.35 (fraction A), 2.95 (fraction B), 3.17 (C), and 4.10 (D), resp. Fraction C was identical (migration compared in various chromatographic systems) with the photoadduct benzo(a)pyrene-thymine obtained after irradiation in previous studies. This photoadduct was obtained with a molecular ratio of 1:7000 with respect to the nucleotides present in the DNA used.

- 0939 INDUCTION OF BENZO[a]PYRENE HYDROXYLASE ACTIVITY IN RAT SKIN. (E.) Schleder, E. (Pharmacol. Inst., Free U. Berlin, Germany) and A. H. Conney. *Life Sci* 9(22):1295-1303, 1970.

The effect of 3-methylcholanthrene (MC) treatment on benzo(a)pyrene hydroxylase activity was investigated in the rat. Five mg of 3-methylcholanthrene was applied topically to the dorsal skin of female rats once daily for 1-3 days. Benzo(a)pyrene hydroxylase activity was assayed and expressed as the formation of 3-hydroxybenzo(a)pyrene. Benzo(a)pyrene hydroxylase activity in untreated controls was uniformly low (5 ng of 3-hydroxybenzo(a)pyrene formed/mg protein/20 min.). A single application of MC increased benzo(a)pyrene hydroxylase activity to 45 ng/mg/20 min in 24 hr. By 2 days after treatment, benzo(a)pyrene hydroxylase had increased to 70 ng/mg/20 min, but thereafter values declined slightly. Benzo(a)pyrene hydroxylase was increased only slightly when the amount of benzo(a)pyrene added to the reaction was increased from 50 μg to 200 μg .

- 0940 EFFECT OF INOCULA OF BENZO[a]PYRENE-TREATED SARCOMA CELLS ON GROWTH OF PRIMARY TUMORS IN RATS. (E.) Hall, J. G. (Chester Beatty Res. Inst., Sutton, Surrey, England) and D. J. Glover. *J Nat Cancer Inst* 45(6):1163-1168, 1970

The effect of inoculating tumor-bearing rats with tumor cells treated with benzo(a)pyrene on the growth of primary tumors was investigated. Fibrosarcomas were induced in rats with s.c. pellets of benzo(a)pyrene, and most of the tumor tissue was removed surgically when the tumors were 1.5-2.5 cm in diameter. Excised tumor cells were exposed to 0.75 mg/100 ml benzo(a)pyrene and caffeine (0.12 mg/100 ml) solution for 20 min at room temperature. Tumor cells were then injected s.c. in the foot pads of the donor rats. The length of time after injection for a primary tumor to increase in diameter by a factor of 1.6 was observed. In control rats receiving only the standard biopsy treatment, the length of time taken for tumors to exhibit this extent of growth was about 15 days (48 days maximum). In rats receiving the tumor cell-benzo(a)pyrene inocula, 18% of the tumors (7/39) had growth periods of more than 100 days. In 5 of these rats, the tumor regressed completely. Three of 7 tumors

this group grew more slowly or regressed after tumor-bearing rat had been inoculated with benzo(a)pyrene-treated allogenic tumor cells. Neither retardation of growth nor regression were observed in rats injected with tumor cells treated with caffeine alone, with nonmalignant mammalian cells or with bacterial cells which had been coated with benzo(a)pyrene. These findings appeared to suggest that benzo(a)pyrene did not act by increasing strength of the tumor-specific antigen, for inoculation of carcinogen-allogenic treated tumor cells and inoculation of carcinogen-treated autologous tumor cells almost the same efficacy in tumor growth retardation.

1 THE RELATION OF METABOLISM TO MACROMOLECULAR BINDING OF THE CARCINOGEN BENZO(a)PYRENE, BY MOUSE EMBRYO CELLS IN CULTURE. (E.) Macan, M. E. (Roy. Cancer Hosp., London, England) and P. Brookes. *Int J Cancer* 6(3):496-505, 1970.

Monolayer cultures of mouse embryo cells were treated with benzo(a)pyrene (BP) and metabolism of the labeled compound (^3H -BP) and its macromolecular binding were observed. The kinetics of BP metabolism were dose-dependent; at concentrations of BP below 2-3 $\mu\text{moles/ml}$ medium, the concentration of metabolized BP decreased exponentially with time. At 6 and 12 hr BP administered in doses of 0.5 $\mu\text{moles/ml}$ had decreased to 70 and 50% of the original concentration, resp. At higher doses of BP there was a period of rapid metabolism followed by a progressive decline. At 6 and 12 hr, BP administered in doses of 10 $\mu\text{moles/ml}$ decreased to 90 and 92% of original concentrations, resp. At low doses of BP the binding of the hydrocarbon to RNA, DNA, and protein was proportional to the overall metabolism, with the result that the binding index, the ratio of bound BP to the amount of BP metabolized, was constant. At higher dose levels of BP, overall metabolism increased with dose, while binding declined off; this resulted in a fall in the binding index value below the constant values found for low doses. The decline in macromolecular binding at high doses of BP appears to preclude a single enzyme mechanism for the metabolism of the hydrocarbon. The findings also appear to suggest that it is the rate of binding of the hydrocarbon rather than its absolute level that is the limiting factor in normal cellular function.

2 ANALYSIS OF ANTIGENIC HETEROGENEITY WITHIN INDIVIDUAL 3-METHYLCHOLANTHRENE-INDUCED SARCOMAS. (E.) Prehn, R. T. (Inst. Cancer Res., Philadelphia, Pa.). *J Nat Cancer* 45(5):1039-1045, 1970.

The differential antigenicity of sections of single mouse sarcomas was investigated. Tumors induced by implants of 3-methylcholanthrene were cloned by moving small sections of tissue from each pole of tumor and establishing clones from each section in syngeneic mice. Test mice were then immunized with clones from each tumor section pair, and 10-15 days later were challenged with tumor cells from the same pair. The growth of the paired subline chal-

lenge tumors was noted weekly. The subline which grew better in immunized animals was arbitrarily designated subline B. There were marked differences in some cases between tumor growth of the 2 sublines in nonimmunized mice. In 1 group of mice, 36% of nonimmunized controls developed tumors of 5 mm in diameter when injected with cells from subline A and 98% of the mice injected with subline B developed tumors of this size. Sublines of a primary tumor appeared to immunize against challenge with cells from that subline rather than against cells from its paired subline. In 1 case, mice immunized with tumor cells of subline A developed tumors in 9% of cases when challenged with tumor cells of subline A; the same mice developed tumors in 42% of cases when challenged with cells of subline B. In this pair of tumor cells, it appeared that the individuality of sublines' antigenicity resulted from a complete lack of demonstrable antigenicity in one of the sublines, rather than from differences in antigenic specificity. In contrast to sublines obtained from primary tumors, sublines taken from 4th and 5th generation tumors showed no differences which might suggest individual specificity between the members of any subline pair. In addition to individual antigenic specificity in the one case, there were cases of cross-reactivity, in which subline B immunized against subline A. Differences in growth potential, immunizing capacity, and responsiveness to immunity were observed between subline pairs in some cases; however, there was no correlation between immunizing capacity of subline and its responsiveness to immunity. Immunizing capacity and responsiveness to immunity appeared to be partially independent variables which varied according to factors other than cellular antigen content. Changes seen during tumor transplantation were thought to be the result of clonal variation subject to selection and operating at random.

0943 PRESENCE OF ANTITUMOROUS AUTOANTIBODIES IN THE BLOOD OF BALB/c MICE WITH METHYLCHOLANTHRENE-INDUCED SARCOMA. (E.) Umansky, Y. A. (Kiev Res. Inst. Exp. Clin. Oncol., USSR), M. I. Federovskaya, E. P. Vetrova and L. P. Kaminskaya. *Neoplasma* 17(5):491-497, 1970.

The blood of mice with sarcomas induced by methylcholanthrene (MC) was examined for the presence of antitumor antibodies. Male mice were injected s.c. with 1 mg of methylcholanthrene; antibody assays were conducted on the blood of these mice before injection with the carcinogen, and subsequently at 1, 2 and 3 months after treatments; test sera were prepared from the same mice. Autoantibodies were found in sera from 16 of 19 tested mice. Three of 16 mice tested proved to be sensitive to the action of antibodies in their own sera by absorption tests. The cytotoxicity of the antibodies in sera from these 3 mice after the induction of tumors decreased proportionally to the increase in the numbers of added tumor cells. With the addition of 20×10^6 tumor cells, the cytotoxic index in mice before treatment, at 2 months after treatment, and at 3.5 months after treatment were 0.45, 0.3 and 0.15, resp. This immunosensitivity appeared at 2-4

months after injection of carcinogen in the 3 mice. Cytotoxicity was determined in the sera of all 19 treated mice; however, no correlation was found between the cytotoxicity of sera and the immunosensitivity of the tumors. Antitumor antibodies did not appear to affect the growth of the methylcholanthrene-induced tumors.

- 0944 3-METHYLCHOLANTHRENE-INDUCED THYROIDITIS IN BUFFALO STRAIN RATS. (E.) Reuber, M. D. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *Arch Environ Hlth* 21(6):734-739, 1970.

The capacity of 3-methylcholanthrene to induce thyroiditis was investigated in Buffalo strain rats. Rats of both sexes were given 0.033% of 3-methylcholanthrene in their food for periods of 4-52 wk. The incidence of rats with thyroiditis increased with continued ingestion of 3-methylcholanthrene. At 4 wk after the commencement of treatment, 8 females had developed thyroiditis, and 1 of them had a severe case. Male rats did not evince severe thyroiditis until 12 wk of treatment (2 cases); however 11 males had thyroiditis 4 wk after the beginning of treatment. By 24 wk, 11/14 females and 8/12 males had severe thyroiditis. Evidently, severe thyroiditis develops suddenly rather than progressing from mild to moderate and then to severe thyroiditis. Protein-bound iodine values in 3-methylcholanthrene-treated rats killed between 4-24 wk were only slightly higher than values for untreated controls.

- 0945 EFFECT OF 3-METHYLCHOLANTHRENE ON HYPERPLASTIC AND EARLY NEOPLASTIC HEPATIC LESIONS INDUCED IN RATS BY CARBON TETRACHLORIDE. (E.) Reuber, M. D. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *J Nat Cancer Inst* 45(6):1237-1242, 1970.

The incidence of liver lesions induced by carbon tetrachloride in Buffalo rats treated with 3-methylcholanthrene (MCA) was investigated. Rats of both sexes aged 5-76 wk were given either carbon tetrachloride (1.3mg/kg s.c.) or MCA (0.033% in feed) or both. The administration of the 2 agents did not markedly affect the survival of rats in the 3 test groups, with survival times ranging from 9-12 wk across test groups. In male rats given carbon tetrachloride only, hepatic hyperplastic nodules began to appear in 8, 24 and 52 wk-old animals; 1 hepatocellular carcinoma developed. Hyperplastic nodules were induced by carbon tetrachloride and MCA in male animals of all ages; carcinomas were seen in rats 12 wk and older. The incidence of nodules and carcinomas increased with age in male animals receiving both agents. More female rats aged 12-52 wk which were given carbon tetrachloride alone developed hyperplastic nodules than did male rats in the same age groups; females of this age group showed the highest incidence of nodules. Carbon tetrachloride and MCA increased the incidence of nodules and carcinomas in females 24, 52 and 76 wk-old more than in males. Rats given carbon tetrachloride alone had fewer lesions/

liver at autopsy than animals given both compounds; cirrhosis was also more severe in rats in the latter group.

- 0946 INDUCTION OF TUMORS IN GUINEA PIGS BY INTRAMEDIASTINAL INJECTION OF METHYLCHOLANTHRENE. (Pol.) Tlolkka-Pluszczyk, J. (Acad. Med. Wroclaw, Poland). *Pat Pol* 21(4):679-696, 1970.

In order to investigate the role of the carrier used for the administration of a carcinogen, methylcholanthrene (MC) was injected as a 3% suspension in gum arabic or bovine serum into the anterior mediastinum of randomly bred 4-10 month-old guinea pigs. Test animals were given single doses of 15 mg MC in 0.5 ml gum arabic (group I, 35 guinea pigs) or 30 mg MC in 1 ml gum arabic (group II, 37 guinea pigs). Groups III and IV were given single doses of 15 mg MC in 0.5 ml or 30 mg in 1 ml of bovine serum (54 and 60 animals, resp.). Group V was given 15 mg MC in 0.5 ml bovine serum twice at a 4 wk interval. Twenty percent of the guinea pigs of group I and 30% of group II developed tumors. None of the guinea pigs of group III, 12% of the guinea pigs of group IV and none of the animals of group V developed tumors. The average weight of the tumors which occurred at different sites was 59 g in the animals of group I, 64 g in the animals of group II and 13 g in the animals of group IV. All the tumors were constituted of single nodules of sarcomatous character, except one which was a chondroblastoma. The carrier used for the administration of MC appears to have a definite effect on the carcinogenic action of methylcholanthrene.

- 0947 INDUCTION OF CANCER BY 20-METHYLCHOLANTHRENE IN DIFFERENT REGIONS OF THE RAT STOMACH. (E.) Arkhipov, G. N. (Acad. Med. Sci., Moscow, USSR). *Cancer Res* 30(11):2739-2743, 1970.

A method of introducing carcinogens into the stomach of mice and rats was developed and employed in tumor-induction experiments in various parts of the rat stomach by 3-methylcholanthrene (3-MC). The carcinogen was placed in an ampul which was pierced with 2, 3 or many holes; the ampul was inserted in the stomach surgically and located in a stomach pocket created by closing off a small area of the stomach wall with a wire fastener. The carcinogen was intended to leach out of the ampul onto the stomach mucosa. It was found that best effects were obtained when 3-MC (5mg) was mixed in the ampul with Vaseline petrolatum jelly as a vehicle; optimum results were achieved with ampuls perforated with 36-40 apertures. Using Vaseline petrolatum jelly and a multi-perforate ampul, 6 adenocarcinomas were induced in the stomachs of 30 rats after 11 wk, while rats given ampuls with fewer apertures developed fewer tumors after longer latencies. In an experiment designed to determine the relative susceptibility of different parts of the rat stomach to tumorigenesis by the ampul method, ampuls containing 3-MC were placed in the forestomach, cardia, fundus and pylorus of rat stomachs (33 animals in each experimental group). After 16 months,

of 27 surviving rats had developed forestomach tumors, 9 of 30 rats had developed tumors in the duodenum area, 2 of 31 rats had developed tumors in the fundus, and 6 of 29 rats had developed tumors in the pylorus. Morphologically, tumors were cornifying squamous cell carcinomas and adenocarcinomas.

3 SPECTROPHOTOMETRIC DETERMINATION OF 20-METHYLCHOLANTHRENE IN DIFFERENT MEDIA. (E.) Vlasov, N. N. (N. N. Petrov Sci. Res. Inst. Biol., Moscow, USSR). *Vop Onkol* 16(9):90-91, 1970.

Spectrophotometric method for the quantitative determination of 3-methylcholanthrene (3-MC) in *n*-hexane soln at λ_{\max} = 295 m μ for the study of its retention and distribution characteristics in experimental carcinogenesis is described. An application of the method is illustrated in a group of rats subjected to surgical implantation of 3-MC (100 μ g) containing paraffin-filled pellets in the bladder wall. Approximately 20% of the 3-MC was removed from the pill 6 months and 40% 12 months after implantation. Urine 3-MC determinations on 12 rats revealed 18-20 ng of 3-MC excretion which corresponded to the decreases observed in the paraffin pills at 6 and 12 months intervals. The method allowed the degree of 3-MC retention within the paraffin pill and the potency of the carcinogenic effect of 3-MC upon the bladder wall to be evaluated. This method can be applied to any carcinogen having a characteristic absorption in the 280-300 m μ region.

4 A LEUKAEMOID RESPONSE IN 3-METHYLCHOLANTHRENE-TREATED RF STRAIN OF MICE. (E.) Kalka, T. (Christie Hosp., Manchester, England) and W. Craig. *Neoplasma* 17(5):499-504, 1970.

Effects of topical epidermal treatment with 3-methylcholanthrene (MC) on mice were investigated. Twenty-two mice (RF) of both sexes and various sub-strains were given a single brush stroke on 4 areas of dorsal skin of MC in a 0.5% solution in benzene. The treated area received an application once every 2 weeks for 20 wk. Fifty-nine of the 72 mice developed squamous cell carcinoma beginning at 84 days after the first treatment. Of these 59 mice, 55 developed a leukemoid reaction. Squamous cell carcinomas of the lungs metastasized only to lymph nodes and lungs. Thirteen mice developed lymphocytic leukemia or lymphoma, mainly of the thymic type; 5 cases of lymphoma were complicated by a severe leukemoid reaction. Major sites of leukemoid reaction were spleen (94% of cases), liver (83% of cases), and lymph nodes (93% of cases). Bone marrow cells from 19 mice diagnosed as having myeloid leukemia were injected i.v. into normal mice. Nine of the recipients developed typical lymphoma after 16-51 days; of the remaining 39 injected mice, 17 were symptom-free 1 yr later. Cell transplantation into syngeneic mice from mice with malignancy was regarded as a valuable practice for determining the essential nature of the malignancy in the donor animals.

0950 CELLULAR ANALYSIS OF RENAL NEOPLASIA: LIGHT MICROSCOPE STUDY OF THE DEVELOPMENT OF INTERSTITIAL LESIONS INDUCED IN THE RAT KIDNEY BY A SINGLE CARCINOGENIC DOSE OF DIMETHYLNITROSAMINE. (E.) Hard, G. C. (Med. Res. Council Lab., Carshalton, Surrey, England) and W. H. Butler. *Cancer Res* 30(11):2806-2815, 1970.

Histogenesis of renal mesenchymal tumors in rats conditioned by a protein-depleted diet and rats fed a casein-supplemented diet was explored through induction of lesions with dimethylnitrosamine utilizing an *in vivo* perfusion fixation technique. A single i.p. dose of 50 or 60 mg/kg dimethylnitrosamine was administered one week after commencement of the protein-free powder diet. At the same time 30 mg/kg dimethylnitrosamine was administered to rats fed the casein-supplemented powder. At selected times rats from each of the experimental groups and the control group were prepared for histological examination. All rats receiving 60 mg/kg dimethylnitrosamine examined at each stage beyond 3 days were found to have interstitial lesions. Ninety percent of protein-depleted rats treated with 50 mg/kg dimethylnitrosamine and 30% of protein-supplemented rats receiving 30 mg/kg possessed interstitial lesions beyond 3 days with no difference in character of lesions found in rats given injections of high or low doses of dimethylnitrosamine. In the control protein-depleted rats, only occasional very early foci of nephropathy at 25 wk were apparent. The first lesions were observed between 2 and 4 days after dimethylnitrosamine treatment with the formation of focal aggregations of cells, invariably near the glomeruli. After the acute response had passed at 7-14 days, hypercellular foci became progressively less and those which persisted showed increase in plasma cells. At 12 wk immunological cells disappeared and the remaining lesions assumed the character of very small tumor cell aggregations, which by 16 weeks had developed into unequivocal microscopic tumors. Mitoses were observed in lesions, most frequently at 7-14 days when the interstitial cell reaction was maximal and from 16 wk when tumor morphology was established. In accord with conclusions of several groups of workers, present results indicate that the various histological forms of dimethylnitrosamine-induced mesenchymal tumors derive from a single cell type near the glomerulus since development is preceded by the same progression of early interstitial change.

0951 THE FORMATION OF VARIANTS WITH A REVERSION OF PROPERTIES OF TRANSFORMED CELLS: V. REVERSION TO A LIMITED LIFE-SPAN. (E.) Rabinowitz, Z. (Weizmann Inst. Sci., Rehovoth, Israel) and L. Sachs. *Int J Cancer* 6(3):388-398, 1970.

The reversion of properties of transformed cells was studied in variants produced by dimethylnitrosamine (DMNA)-transformed hamster embryo cells. Variant cells were flat epithelioid cells compared to the parental transformed cells which were fibroblastic with a random growth pattern. Fixed normal cells provided 16-44% variants which were inhibited

by cells from the same clone or from another variant and by the parental transformed cells. The variants had lower saturation density ($3-4 \times 10^6$ cells) than the parental cells ($12-14 \times 10^6$ cells) as well as lower cloning efficiencies in fluid medium (3-11% compared to 71%) and in soft agar (0.1-5% compared to 31%); inoculation (s.c.) of 10^6 variant cells was required to parallel the *in vivo* tumorigenicity of 10^3 parental transformed cells. Subcultured transformed cells remained viable on fixed normal cells or feeder layers, but 81-85% of the variants from DMNA-transformed cells and 87-93% of the variants from benzo(a)pyrene- or X-irradiation-transformed cells terminated their life-span; only 5% of the variants from polyoma virus-transformed cells lost their viability. Escape from the limited life-span (which was determined intracellularly) by 15-19% of the variants from the DMNA-transformed cells was due to a re-reversion from the reverted to the transformed state.

- 0952 CELLULAR ANALYSIS OF RENAL NEOPLASIA: INDUCTION OF RENAL TUMORS IN DIETARY-CONDITIONED RATS BY DIMETHYLNITROSAMINE, WITH A REAPPRAISAL OF MORPHOLOGICAL CHARACTERISTICS. (E.) Hard, G. C. (Med. Res. Council Lab., Carshalton, Surrey, England) and W. H. Butler. *Cancer Res* 30(11):2796-2805, 1970.

The development of renal tumors in rats treated with dimethylnitrosamine (DMN) and maintained on protein-deficient and protein-supplemented diet was investigated. Male rats were given either a protein-free diet, a diet containing 30% protein (casein), a normal diet, a diet of sucrose granules for 1 wk or were starved for 64 hr. All groups were then given injections of 30-60 mg DMN; the rats on the protein-free diet were kept on that for 1 wk more and then returned to a normal diet; all other animals were put on normal diets after DMN administration. A quarter of the rats given conventional diet survived the administration of 60 mg DMN, while 44% of protein-depleted rats given 60 mg and 58% of those given 50 mg survived the initial toxic reaction to the carcinogen. All protein-depleted rats given 60 mg DMN developed renal epithelial tumors (4 adenocarcinomas and 13 mesenchymal tumors). Eighty-seven % of protein-depleted rats given 50 mg DMN developed tumors, and only 28% of rats fed with protein-supplemented food and given 30 mg DMN developed tumors. Rats on the conventional diet given 60 mg DMN developed tumors in 35% of cases, while the percentage of animals developing tumors among those given sucrose granules and 50 mg DMN was 89%. Starved rats given 50 mg DMN developed tumors in 86% of cases, while uninjected controls who had been given a protein-deficient diet developed no tumors. There were 96 mesenchymal tumors and 27 adenocarcinomas in 116 DMN-treated animals. The DMN-induced renal mesenchymal tumors apparently were not nephroblastomas, and all epithelial components other than independently developed adenomas or adenocarcinomas were consistent with pathologically-altered pre-existing renal parenchyma. Mesenchymal tumors appeared to differentiate into the various components of vascular tissue including spindle-shaped, fibro-

blast-like cells, smooth muscle cells, and vascular channels.

- 0953 RESPONSIVENESS OF NORMAL AND TRANSFORMED RAT EMBRYO CELL CULTURES TO POLY I-POLY C AND INTERFERON. (E.) Freeman, A. E. (Microbiol. Assoc., Bethesda, Md.), C. P. Uhlendorf, P. E. Younkers and S. Baron. *J Cell Physiol* 76(3):365-372, 1970.

In the present study a number of normal, virus-infected, and transformed (spontaneous or diethylnitrosamine-induced) pooled Fischer rat embryo cell lines were tested for responsiveness to the interferon inducer, polyinosinic-polycytidylic acid (poly I-poly C) and to exogenous interferon. Of the three cell pools assayed at two subculture levels, one culture lost its responsiveness to poly I-poly C and to interferon upon subculture; a second was more responsive; a third became more sensitive to interferon only. Degree of sensitivity of rat cells to poly I-poly C was independent of treatment and of morphological transformation and was unrelated to virus infection. The interpretation is that the degree of interferon responsiveness influences the rate of transformation but is not an absolute requirement of cellular transformation.

- 0954 INCREASED RENAL CARCINOGENESIS BY DIMETHYLNITROSAMINE IN PROTEIN DEFICIENT RATS. (E.) McLean, A. E. M. (U. Coll. Hosp. Med. Sch., London, England) and P. N. Magee. *Brit J Exp Path* 51(6):587-590, 1970.

The effect of a protein-deficient diet on the development of renal carcinomas in rats given dimethylnitrosamine was investigated. Male rats were fed a protein-free diet for 7 days before being given a single i.p. dose of 60 mg/kg dimethylnitrosamine. All 14 of the surviving rats developed renal tumors between 8-11 months after dimethylnitrosamine injection. Tumors were multifocal in many cases and originated from the epithelium or interstitial cells. Two pulmonary adenomas were also found. None of the untreated controls had developed tumors at 7 months. When animals injected with dimethylnitrosamine were given phenobarbital and/or DDT doses, it was found that phenobarbital did not protect against the carcinogenic action of dimethylnitrosamine; 3 of 3 rats fed a protein-free diet and given phenobarbital developed tumors and 1 of 2 rats fed a protein-free diet and given DDT developed tumors.

- 0955 ULTRASTRUCTURE OF LIVER CELL CARCINOMA IN *MACACA MULATA* MONKEY. (E.) Williams, A. C. (Dept. Path., U. Ibadan, Nigeria). *Exp Molec Path* 13(3):359-369, 1970.

Four hepatocarcinomas induced by N-nitrosodiethylamine in rhesus monkeys were examined under the electron microscope; 2 of the tumors were well-differentiated carcinomas, and 2 were poorly differentiated carcinomas. Monolayer and suspension cell cultures of tumor cells were also examined. Well-differen-

ated carcinomas had scanty rough endoplasmic reticulum and abundant free ribosomes. Rough cisterns occasionally enveloped mitochondria. The cristae sometimes traversed the width of the mitochondria, producing a dumb-bell effect. Microbodies were not frequent in well-differentiated carcinomas as in poorly-differentiated carcinomas. Large vacuoles were not uncommon, and lipid bodies were sometimes frequent. The hepatic cell membranes had microvilli. Most nuclei were rather large, with irregular outlines. Poorly-differentiated hepatocarcinomas had abundant smooth endoplasmic reticulum and smaller mitochondria with fewer cristae than the mitochondria of the well-differentiated tumors. Poorly-differentiated tumors had less well-developed and less orderly cytoplasmic organelles than well-differentiated tumors, including mitochondria and ergastoplasm.

- 56 ANTIGENICITY OF DIETHYLNITROSAMINE-INDUCED RAT HEPATOMAS. (E.) Garisoain, M. (Felix Huarte Ctr. Biol. Invest., U. Navarra, Complona, Spain) and J. M. Arcos. *Acta Oncol* 11:40-47, 1970.

The antigenicity of diethylnitrosamine-induced (approximately 4.2 mg/kg/day, p.o.) rat hepatomas was studied by immunoelectrophoresis and precipitin reactions. Direct immunoelectrophoretic analysis of the hepatoma against anti-normal liver immunoserum and against anti-hepatoma immunoserum yielded complex patterns similar to those obtained with normal livers. A specific hepatoma antigen (DEN-86) not found in normal liver homogenates was observed with relative electrophoretic mobility of 86%. DEN-86 is not glycidic or lipid in nature, showed no esterase activity, and had a high resistance to temperature and ultrasonic vibrations (20 min at 100°C and 60 min of ultrasonic vibration did not significantly alter the antigen). Preliminary localization tests indicated that the antigen sedimented in the nuclear fraction (700 x g), but after violent centrifugation of the hepatoma (Ultra-turrax at 15,000 rpm for 5 min) the antigen did not sediment after 1 hr at 150,000 x g.

- 57 SPECIFIC CHANGES IN CELLULAR RESPONSE TO HOMEOSTATIC CONTROL DURING DIETHYLNITROSAMINE-INDUCED LIVER CARCINOGENESIS. (E.) Rabes, R. (Pathologisches Institut der Universität, München, Germany) and P. Scholze. *Experientia* 26(12):1356-1359, 1970.

The growth behavior of preneoplastic liver cells was studied in rats following the administration of 100 mg of diethylnitrosamine (DEN) daily in drinking water; some rats were partially hepatectomized. Methylated thymidine (100 µC injected i.p.) was used to monitor DNA synthesis. By 10 days after the start of DEN treatment, the growth fraction of liver cells showed characteristic changes; glucose-6-phosphatase and adenosine triphosphatase activity were most pronounced around the portal field, falling off toward the lobular center. Cells in DNA synthesis were restricted to areas of highest enzyme activity, and there were no DNA synthesizing cells

in the area encircling the central vein of the liver. Both DNA synthesis and enzyme activity in these areas were restored when carcinogen-feeding was discontinued. After 40 days of DEN feeding, the areas of complete enzyme deficiency became sharply circumscribed. Simultaneously with the loss of enzyme activity, cells regained their ability to respond to homeostatic regulation. After partial hepatectomy, 90% of cells in the enzyme-deficient areas were labeled with tritiated thymidine. Liver cells, which were considered preneoplastic, showed little proliferation until 90 days after the start of DEN feeding in the absence of a growth stimulus; when a growth stimulus was provided by partial hepatectomy, however, they proliferated rapidly. Transformation of prospective tumor cells into autonomous hepatomas apparently proceeded in 3 stages: a stage of reduced enzyme activity coincident with loss of ability to proliferate; a stage of complete loss of enzyme activity in acinocentrally located groups of cells coincident with a return of the ability to proliferate, which was usually confined to cells provided with a proliferation-stimulus (partial hepatectomy); and a stage of autonomous proliferation of these enzyme-poor cells without additional growth stimulus.

- 0958 RESPONSE OF ADULT MASTOMYS (*PRAOMYS NATALENSIS*) TO SUBCUTANEOUS INJECTION OF N-NITROSODIMETHYLAMINE. (E.) Fujii, K. (Nat'l. Inst. Hyg. Sci., Tokyo, Japan) and H. Sato. *Gann* 61(5):425-434, 1970.

Tumorigenesis induced by the carcinogen N-nitrosodimethylamine in mastomys (*Praomys natalensis*) was investigated. Animals were given s.c. injections of the carcinogen twice a wk for 10, 19, 27, 36, and 44 wk in doses totaling 2.0, 3.8, 5.4, 7.1 and 8.8 mg. Males treated for more than 27 wk showed shorter mean survival times than males treated for less than 19 wk, an effect not noted for females. Mean survival for males treated for 19 wk was 56 wk, and 23 wk for males treated for 36 wk. Liver tumors developed in 4 untreated females and in 7 treated males; none of the treated females developed liver tumors. Tumors in controls were diagnosed as hepatocellular carcinoma or hyperplastic nodules, while tumors developing in treated animals included cholangiocystadenoma or cholangiocarcinoma; average latent periods for liver tumors in treated animals were 53-56 wk. Incidences of stomach tumors in treated males were from 33-41%. The incidence and latent period of liver tumors did not show dose correlations, and the incidence of stomach tumors in treated males was lower than in untreated males. Other tumors found in treated mastomys included pituitary adenoma, thymic lymphoma and adrenal adenoma.

- 0959 THE EFFECT OF PARTIAL HEPATECTOMY ON DIETHYLNITROSAMINE HEPATOCARCINOGENESIS IN RATS. (Ger.) Grünthal, D. (Gyn. Clin. Univ. Hamburg, Eppendorf, Germany) D. O. Hellenbroich, P. Sängner, and H. Maass. *Z Naturforsch* 25 b(11):1277-1281, 1970.

The effect of regeneration processes following partial hepatectomy on diethylnitrosamine (DENA) hepatocarcinogenesis was studied in 2 sets of experiments with female Wistar rats. In the first experiment, total survival time was determined in: A) 10 rats subjected to a 2/3 hepatectomy at the beginning of DENA treatment (2 mg daily in drinking water till termination); B) 10 rats subjected to a similar hepatectomy after 86 days of DENA intake; and C) 10 rats exposed to DENA treatment without hepatectomy. In the second experiment, 60 rats were subjected to 5 partial hepatectomies and intermittent DENA treatment as follows: D) 24 rats were subjected to partial hepatectomy and subsequently given DENA; E) 24 rats were given 9 mg/kg DENA in drinking water 1 wk after partial hepatectomy for 3 consecutive days; and F) 12 rats were given DENA under similar conditions as group E but without hepatectomy. Partial hepatectomies were performed subsequently at 14 day intervals with a 4 wk interval after the 3rd operation. DENA was given after each operation (3.9 mg/kg daily with 14 day intervals for 28 wk) until a total of 351 mg/kg per rat was administered. The average survival time in the first experiment decreased from 225 days (control group C to 158 days in group A), and all the animals developed liver carcinomas. In the second experiment the mitotic rate in group D was 70% higher (not significant) than in group E. Histological investigation of resected liver segments from live and dead rats showed (according to Grundmann and Sieburg) conditions referred to as stage I through the 6th wk, stage IIa between the 10th-18th wk and stage IIa-IIb between the 20th-28th wk of the experiment. Of the 20 surviving rats at the 40th wk of the experiment, 3 rats from group D had dedifferentiated carcinoma, 1 rat from group E had a partially dedifferentiated carcinoma and in group F 9 rats developed microcarcinomas while only 2 rats developed carcinoma. Enzyme activities (phosphorylating enzymes and the LDH/GPDH ratio) in premalignant tissues showed no differences from normal liver tissue. However, the proliferative processes during liver regeneration seemed to promote DENA hepatocarcinogenesis.

0960 HISTOCHEMICAL INVESTIGATIONS IN RAT LIVER DURING DIETHYLNITROSAMINE HEPATOCARCINOGENESIS. (Sp.) Hernandez, F. (Fac. Med. U. Navarre, Spain) and J. Martinez de Morentin. *Rev Med Univ Navarra* 13(2):175-183, 1970.

Histochemical investigations of malate, lactate, glutamate, succinate, β -hydroxybutyrate and α -glycerophosphate dehydrogenases, NADH and NADPH dependent diaphorases, acid and alkaline phosphatases, nonspecific esterases and ubiquinone were made in liver tissues during diethylnitrosamine (DENA) carcinogenesis in Wistar rats given 5 mg DENA/kg p.o. daily for 22 wk. During this period 1 control and 3 treated rats were sacrificed weekly. The first nodules of hepatoma appeared on the 18th wk of the experiment. Two distinct stages in DENA carcinogenesis were noticed: the first stage lasted 10-14 wk and was characterized by a decrease in Krebs cycle specific enzymes such as succinate, glutamate

and malate dehydrogenases, while lactate and α -glycerophosphate dehydrogenases were unchanged. The second stage of the process (between wk 10-14 through wk 22) was characterized by an increase in β -hydroxybutyrate dehydrogenase (related to fatty acid metabolism) and α -glycerophosphate dehydrogenase (glycolysis) and in alkaline phosphatase (membrane transport mechanisms) occurring in isolated preneoplastic cell groups. No differences in diaphorase and ubiquinone levels were noticed. A decrease in acid phosphatase was noticed beginning from the 8th wk of the experiment within the lysosomal areas. The hepatoma tissues exhibited generally low levels of these enzyme activities. The role of acid phosphatase in DENA carcinogenesis is discussed.

0961 CELLULAR INJURY AND CARCINOGENESIS: INHIBITION OF METABOLISM OF DIMETHYLNITROSAMINE BY AMINOACETONITRILE. (E.) Fiume, L. (Max Planck Inst. Med. Res., Heidelberg, Germany), G. Campadelli-Fiume, P. N. Magee and J. Holsman. *Biochem J* 120(3):601-605, 1970.

The inhibition of dimethylnitrosamine by aminoacetonitrile was investigated in rat liver *in vivo* and in rat liver slices *in vitro*. The rate of disappearance of dimethylnitrosamine from the circulating blood of rats to which it had been administered in doses of 30 mg/kg body wt was decreased by treatment of the animals with aminoacetonitrile (200 mg/kg body wt). Rats receiving dimethylnitrosamine alone had blood levels of 4 μ g/ml at 6 hr after administration, while rats given aminoacetonitrile and dimethylnitrosamine did not exhibit this level of dimethylnitrosamine in the blood until 47 hr after treatment. Aminoacetonitrile also inhibited metabolism of dimethylnitrosamine *in vitro*. The methylation of rat liver and kidney nucleic acids *in vivo* by 14 C-dimethylnitrosamine showed that aminoacetonitrile inhibited the incorporation of the labeled compound into proteins of both organs 4-12 hr after injection. Four hr after treatment, the labeled dimethylnitrosamine content of rat livers without aminoacetonitrile was 120 cpm/mg, while that for rats given aminoacetonitrile was 48 cpm/mg. The observed inhibition of dimethylnitrosamine metabolism by aminoacetonitrile explains the ability of this agent to prevent the appearance of dimethylnitrosamine-induced liver tumors.

0962 CARCINOGENICITY OF A SINGLE ADMINISTRATION OF N-NITROSOMETHYLUREA: A COMPARISON BETWEEN NEW-BORN AND 5-WEEK-OLD MICE AND RATS. (E.) Terracini, B. (Inst. Anat. Path., U. Turin, Italy) and M. C. Testa. *Brit J Cancer* 24(3):588-598, 1970.

The carcinogenic effects of N-nitrosomethylurea (NMU) on newborn and weaned mice and rats was investigated. Hybrid mice (C57BL x C3Hf) F_1 and Wistar rats were given a single i.p. injection of NMU (50 μ g/g body wt) when newborn or at 5 wk of age. Eleven of 95 mice treated at birth died before weaning compared with 3 of 34 untreated controls; early deaths did not occur among mice treated at 5 wk. Body growth in mice treated at

Birth was consistently impaired; the wt of treated mice at 50 wk-of-age was 17 g, while the wt of controls at this time was 30 g. Seven percent of mice treated at birth and 21% of mice treated at 5 wk were tumor free, compared to 97% of controls. Of the male mice treated at birth, 58% had lymphosarcomas, 80% had lung adenomas, 84% had hepatomas, and 20% had renal adenomas. Of the male mice treated at 5 wk of age, 31% had lymphosarcomas, 40% had lung adenomas, none had hepatomas, 9% had renal adenomas, and 36% had tumors of the forestomach. The pattern of tumor occurrence was similar in female mice except for a higher incidence of forestomach tumors and a lower incidence of hepatomas (5% in female mice treated at birth). Growth depression comparable to that seen in mice occurred in NMU-treated rats. In male rats treated with NMU at birth, incidences of 10% lymphosarcomas, 77% renal anaplastic tumors, 21% renal adenomas, 28% forestomach tumors, and 30% intestinal adenocarcinomas were seen; similar tumor incidences were found in female rats except for 50% forestomach tumors, 100% intestinal adenocarcinomas, and 28% mammary tumors. Female and male rats injected at 5 wk-of-age developed 9% and 75% lymphosarcomas, 8% and 54% renal anaplastic tumors, 0% and 25% renal adenomas, no forestomach tumors, 0% and 50% intestinal adenocarcinomas, and 60% and 0% mammary tumors, resp. Multiple tumors in the same animal were frequently seen. Since NMU breakdown is rapid and may not require an enzyme, it seems that factors other than the degree of maturation of enzyme production are responsible for the differential susceptibility among newborns and young adult mice to carcinogenesis by this compound.

963 EXPERIMENTAL BRAIN TUMOURS INDUCED IN RATS BY NITROSOUREA DERIVATIVES: I. MORPHOLOGICAL ASPECTS OF METHYLNITROSOUREA TUMOURS. (E.) Schiffer, D. (Clin. Nerv. Mental Dis., U. Turin, Italy), P. Fabiani, E. Grossi-Paoletti and P. Paoletti. *J Neurol Sci* 11(6):559-572, 1970.

Long Evans male rats received 25 mg/kg of methylnitrosourea by injection in the tail vein once a month for 6 months, starting in the second month of life. Twenty-nine (80%) of 36 treated animals developed neoplasms of the brain; 12 rats had a solitary tumor, 6 of which were glial, and 17 animals had multiple tumors. Forty-eight of the tumors were intracranial tumors and included 17 oligodendrogliomas, 5 isomorphous gliomas, 10 polymorphous gliomas, 10 glial foci, 2 neurinomas, 2 sarcomas, an epithelial cyst, a plexus papilloma and a spinocellular carcinoma. Eight spinal tumors were also found; these included 4 isomorphous gliomas, 1 polymorphous glioma, a glial focus and 2 neurinomas.

964 EXPERIMENTAL BRAIN TUMOURS INDUCED IN RATS BY NITROSOUREA DERIVATIVES: II. MORPHOLOGICAL ASPECTS OF NITROSOETHYLUREA TUMOURS OBTAINED BY TRANSPLACENTAL INDUCTION. (E.) Grossi-Paoletti, P. (Inst. Pharmacol., U. Milan, Italy), P. Paoletti, D. Schiffer and A. Fabiani. *J Neurol Sci* 11(6):573-581, 1970.

Long Evans female rats were given 10 mg/kg of ethylnitrosourea i.v. on the 17th day of pregnancy; the 46 offspring, which appeared normal at birth, were sacrificed 150-400 days later, and the pathology of the central nervous system was studied. Fifty-eight neoplastic proliferations of cells were observed in 41 of 46 treated rats (89%). The occurrence of multiple tumors increased as the time interval before sacrifice was increased. Forty intracranial tumors (21 neurinomas, 11 oligodendrogliomas, 6 oligodendroglial foci, and ependymoma and a glioblastoma) and 18 spinal tumors (14 neurinomas, 3 oligodendrogliomas and an ependymoma) were found. Neurinomas of the Gasserian ganglion and spinal neurinomas were the first to occur; multiply associated neurinomas and neurinomas occurring with oligodendroglial hyperplasia followed by oligodendrogliomas were next to be seen. Three of the 21 Gasserian ganglion neurinomas and 1 of the 13 spinal neurinomas showed characteristics of high histological malignancy.

0965 NERVE TUMORS EXPERIMENTALLY INDUCED BY APPLICATIONS OF N-METHYL-N-NITROSOUREA IN RATS: III. ELECTRON MICROSCOPIC STUDIES. (Ger.) Jänisch, W. (Med. Acad. Erfurt, Germany), A. Lageman, W. Dietz and D. Schreiber. *Exp Path* 4(5-6):317-328, 1970.

An electron microscopic investigation of the histogenesis of 10 experimentally induced tumors of the peripheral nerves and spinal nerve roots in rats is presented. Of these, 9 resulted from the i.v. injection of N-methyl-N-nitrosourea (10-25 mg/kg 2-4 times weekly), and in another rat a tumor of the cauda equina, of the lumbosacral plexus, and of both adrenals was produced with ethylnitrosourea. Three types of growth were distinguished in these tumors. The first group included those parts of the tumor with loose cell formation and wide intracellular spaces. Most of these cells were surrounded by basement membranes from which long thin processes protruded. These lamella-shaped processes were partially isolated and found in thick layers in the intercellular space. The nuclei of these cells were oblong and showed deep grooves. These cells were associated with tumors derived from Schwann's cells, in which a definite sign of abortive medullary formation was demonstrable in the tumor cells. The second group of findings comprised those tumors diagnosed by light microscopy as anaplastic tumors, and differed from the tumors in the first group in 2 ways: they were characterized by very few cells with a basement membrane, and the cell processes were short. No specific ultrastructural features could be found in these, and it is inconclusive whether these tumors were derived from the Schwann's cells as well. The third group was distinguished by the thick processes associated with the cells; they were thickly packed and ran parallel to each other and were often surrounded by a common basement membrane. The medullary sheaths were absent. These cells may be derived from a perineural origin.

0966 LACTIC DEHYDROGENASE ACTIVITY AND ISOENZYME PATTERNS IN EXPERIMENTAL TUMORS OF THE PERI-

PERIPHERAL NERVOUS SYSTEM OF THE RAT. (Ger.) Stavrou, D. (Med. Fac. Munich, Germany), M. Knedel and H. Kirzeder. *Ges Exp Med* 153(3):223-233, 1970.

The distribution of lactate dehydrogenase (LDH) and its isozymes and their electrophoretic separation from 22 experimentally induced neurinomas in rats is described. One group of 100 Sprague-Dawley rats was injected s.c. with 50 mg/kg phenyldimethyltriazine weekly, and a second group of 100 rats was supplied with drinking water providing 6 mg/kg N-methyl-N-nitrosourea (MNH) twice weekly, following a 12 hr period of water deprivation. The tumors investigated included nerve root neurinomas of the spine and cerebral nerves, as well as those of the cauda equina. The intensity of LDH activity varies from tumor to tumor and even within different areas of the same tumor, but this activity does not differ greatly in tumors which are similar in construction. High enzyme activity was found in reticular tumor sections, and LDH-positive cytoplasm was seen lying close to the nuclei. High enzyme activity was also seen in slightly vascularized tumor areas in contrast to a low activity in the highly vascularized areas. Agar gel electrophoretic separation of the LDH isozyme in the normal nerves of the rat showed 5 isozymes, with the cathodic isozyme LDH₅ having the highest activity. However, all 5 isozymes were not detectable in most of the tumors; the anodic LDH₁ band was usually negligible and the cathodic LDH₅ band showed highest activity.

0967 ELIMINATION, TISSUE ACCUMULATION, AND METABOLIC FATE OF 4-NITROQUINOLINE-1-OXIDE ADMINISTERED ORALLY IN RATS. (E.) Kato, R. (Natl. Inst. Hyg. Sci., Tokyo, Japan), A. Takahashi, W. Ngamwatana and Y. Omori. *Gann* 61(5):415-424, 1970.

The elimination, tissue accumulation, and metabolic fate of ³H-labeled 4-nitroquinoline-1-oxide was investigated in rats. Male rats were given ³H-4-nitroquinoline-1-oxide orally (15 mg/kg) and killed from 1-96 hr later, at which times the accumulation of the radioactive label in various organs and its elimination were observed. Radioactive substances were excreted through both fecal and urinary routes; in 48 hr, 57% of radioactive label was eliminated through the urine and 30% through feces. After 48 hr, excretion of the label from fecal and urinary routes was approximately equal. Total recovery from urine and feces of radioactive substances was about 90% of the oral dose. At 24-96 hr after administration, the stomach tissues contained 3-5 times more radioactivity than did other organs (136 cpm x 10³/g wet wt). Radioactivity was concentrated in the forestomach which contained about 82% of the total radioactivity in stomach tissue; specific activity was higher in the mucosa of the forestomach than in forestomach muscle tissue. Thin layer chromatography of extracts of each tissue was performed with acidic ethanol with the result that the radioactivity in the 4-nitroquinoline-1-oxide fraction was low in stomach tissues after 12 hr (4.8%). Radioactivity in the 4-aminoquinoline-1-oxide fraction was high in stomach tissues after 12

hr (48.8%), but radioactivity interacting with proteins and nucleic acids was not so high in liver and intestine as in stomach tissues.

0968 DNA REPAIR AND CHROMATID ANOMALIES IN MAMMALIAN CELLS EXPOSED TO 4-NITROQUINOLINE-1-OXIDE. (E.) Stich, H. F. (Cancer Res. Ctr., U. British Columbia, Vancouver, Canada) and R. H. C. San. *Mutat Res* 10(4):389-404, 1970.

DNA-repair synthesis (unscheduled DNA synthesis) was followed in normal, diploid, aneuploid, and neoplastic human and hamster cells after exposure to 4-nitroquinoline-1-oxide (4NQO). DNA-repair synthesis was separated from DNA-replication synthesis associated with chromosome replication at S-phase by maintaining the cultures in an arginine-deficient medium before 4NQO exposure. All of the cell types tested showed a high capacity for DNA-repair synthesis (94-100% of the nuclei incorporated ³H-thymidine), but the amount of incorporation into nuclear DNA of cells exposed to 4NQO depended on the dose of 4NQO (5 x 10⁻⁸ to 1 x 10⁻⁵M) and on the amount of DNA in the cell. A time course study of 4NQO-induced (5 x 10⁻⁶M for 1.5 hr) repair synthesis indicated that the synthesis was at a maximum (120-130 grains/nucleus) 2-4 hr after treatment and that it fell off rapidly thereafter to a near steady state rate (10-20 grains/nucleus). Cells were capable of starting with DNA replication at S-phase without having completed the DNA-repair synthesis, but passage of the cells from G₂ to metaphase was severely inhibited (80%) by 4NQO at 10⁻⁶M concentrations. Chromosomal responses to 4NQO included loosening of the coiled structures, single isochromatid and multiple breaks, and single and multiple chromatid exchanges.

0969 TUMORIGENIC EFFECT OF THIOACETAMIDE IN SWISS STRAIN MICE. (E.) Gothoskar, S. V. (Cancer Res. Inst., Bombay, India), G. V. Talwalkar and S. V. Bhide. *Brit J Cancer* 24(3):498-503, 1970.

The effect of treatment with thioacetamide on the livers of Swiss mice was investigated. Mice were fed a diet containing 0.03% thioacetamide, and livers were examined 6, 9, 13 or 17 months after commencement of treatment. Gross changes in the appearance of the liver, including granularity, increased liver wt, and darkened color were discernible in mice autopsied 13 months after the beginning of thioacetamide treatment. Nodular areas were seen on livers of mice killed after 17 months of treatment; no secondary lesions in other organs could be found in this group, however. In mice killed 6 months after beginning thioacetamide treatment, microscopic examination showed mild generalized hypertrophy of the hepatic cells; hypertrophy was more marked in the 9 month group in which bile-duct proliferation was observed. Mice killed after 13 months of treatment showed cirrhosis and cholangiofibrosis in 1 case. In this group, all treated males and 6/7 of the treated females developed hepatomas. Transplantation of these tumors to mice of the same strain produced palpable tumors

n 4-6 months. Both RNA and DNA levels in thioacetamide-treated liver tissue were comparable with levels in corresponding control groups. However, RNA and RNA levels in tumor tissue in males were significantly higher than those in the corresponding control livers; in mice killed 17 months after commencement of thioacetamide treatment, RNA levels in tumors were 0.25 μg of nucleic acid/ μg of protein, compared to 0.15/ μg in the controls. In the same experimental group, DNA levels were 0.20 μg nucleic acid/ μg protein while control values for DNA were 0.15 μg / μg protein.

970 STUDIES ON PROGRESSIVE METABOLIC ALTERATIONS IN THIOACETAMIDE INDUCED HEPATOCARCINOGENESIS. (E.) Bhide, S. V. (Cancer Res. Inst., Tata Mem. Ctr., Parel, Bombay, India). *Brit J Cancer* 24(3):504-509, 1970.

Progressive metabolic alterations in liver tissue of mice treated with thioacetamide were investigated; metabolic parameters studied included glycogen and lactic acid levels, glucose-6-phosphatase, fructose-1-6-diphosphatase, aldolase, aspartic and ornithine transcarbamylase, arginase, and xanthine oxidase activities. Mice were fed 0.03% thioacetamide in a normal diet. Glycogen content in treated mice decreased significantly from the age of 4 months; at this point glycogen content in control mice and thioacetamide-treated mice were 60.53 and 41.81 μg glucose/mg tissue, resp.; lactic acid levels in treated mice exceeded those in controls, with the change becoming evident at 9 months when lactic acid levels in control and treated mice were 1.2 and 4.8 μg lactic acid/mg tissue, resp. Glucose-6-phosphatase and fructose-1-6-diphosphatase activities were decreased in treated mice from the age of 4 months; the extent of decrease in enzyme activities in host liver and tumor were comparable. Thioacetamide treatment caused an increase in aldolase activity from the age of 9 months when aldolase activity values in control and treated mice were 0.9 and 1.3 μg triose-phosphate liberated/hr/mg tissue, resp. Aspartic transcarbamylase activity in treated mice increased from the age of 9 months, while ornithine transcarbamylase activity in treated mice decreased from the age of 13 months. Xanthine oxidase and arginase activity decreased in treated mice from the age of 9 months. Maximum changes in enzyme activities were observed in hepatomas at the age of 17 months.

0971 LIVER REGENERATION AND INDUCTION OF HEPATOMAS IN B6AF₁ MICE BY URETHAN. (E.) I. N. Chernozemski (Roy. Cancer Hosp., London, England) and G. P. Warwick. *Cancer Res* 30(11):2685-2690, 1970.

The effect of urethan injections on hepatoma formation in hepatectomized mice was investigated. Male and female mice were hepatectomized by a procedure which removed 63-69% of the liver. Hepatectomy was followed by urethan injections (1 mg/kg body wt) at 4-5 hr after surgery (i.e., at the early pre-replicative period for regenerating liver cells), at

17-18 hr after surgery (i.e., during the late pre-replicative period), at 31-33 hr after surgery (i.e., shortly before the onset of extensive regenerative DNA duplication), or at 46 hr after surgery (i.e., before the peak of mitosis in regenerating cells). One untreated control (no surgery, no urethan) developed a hepatoma (3.3% incidence), and 6 mice which had hepatectomies but no chemotreatment developed hepatomas (19% incidence). Among mice given urethan but not hepatectomized, 2 hepatomas developed (6% incidence), while among mice given urethan 4-5 hr after hepatectomy, 2 tumors developed (10% incidence). Of mice given urethan 17-18 hr after hepatectomy, 17 developed hepatomas (68% incidence); of those treated 31-33 hr after surgery, 11 developed tumors (52% incidence). Of mice given urethan 46 hr after hepatectomy, 20 developed hepatomas (77% incidence). The largest average number of tumors developed/mouse was 1.9 in mice of the group given urethan 17-18 hr after hepatectomy. Most of the mice developing tumors were males.

0972 ENHANCED METHODS OF DETECTION OF BLASTOGENIC PROPERTIES OF CHEMICAL COMPOUNDS: EXPERIMENTS WITH URETHAN. (Rus.) Zadorozhnaya, N. A. (All-Union Res. Inst. Hyg. Toxic. Pesticides, Polymers, Plastics, Kiev, USSR) and O. P. Chepinoga. *Vop Onkol* 16(9):71-73, 1970.

Experimental models were tested with urethan in order to establish faster methods for studies of chemical carcinogenesis; the effect of urethan in randombred white mice in the prenatal period was compared to effects produced at 2-3 months-of-age. The experimental mice were given urethan (1 mg/g body wt, i.p.) on the 17th and 19th day of pregnancy. The newborn mice were observed for 3 months at which time half of each progeny were sacrificed, and half were subjected to additional urethan treatment for 3 months (1 mg/g body wt on alternative days). These mice were then sacrificed at 6 months of age and examined for cancer incidence. An additional 2 groups of 3 month-old normal mice were given urethan 2 and 5 times (2 and 5 mg/g wt, resp.) on alternative days. Lung adenomas were found in 50% of the 3 month-old progeny of transplacentally treated animals and in 4% of the control mice. Additional urethan administration to the 3 month-old animals of this group produced adenomas in 88% of the mice at 6 months of age. The incidence of adenomas in the twice treated normal animals was 63% in 3 months. Higher doses (5 administrations) of urethan under similar conditions produced 90% tumor incidence in 3.5 months and seemed to constitute the most appropriate experimental model.

0973 EFFECTS OF CIGARETTE SMOKING ON DOGS: I. DESIGN OF EXPERIMENT, MORTALITY, AND FINDINGS IN LUNG PARENCHYMA. (E.) Hammond, E. C. (American Cancer Soc., New York, N.Y.), O. Auerbach, D. Kirman and L. Garfinkel. *Arch Environ Hlth* 21(6):740-753, 1970.

The effects of smoking filtered and unfiltered cigarettes on mortality, cause of death, and neoplastic development were investigated in beagle dogs.

Eighty-nine dogs were trained to smoke cigarettes through a tracheostoma, and were then given cigarettes over a test period of 875 days as follows: 6,143 filtered cigarettes, 3,103 unfiltered cigarettes, 6,129 unfiltered cigarettes, and no cigarettes (nonsmoking controls). Tar contents of filtered and unfiltered cigarettes were 17.8 and 34.8 mg tar, resp., and the nicotine contents of filtered and unfiltered cigarettes were 1.17 and 1.85 mg nicotine, resp. None of the nonsmoking dogs died before day 875; 2 of 12 filtered cigarette smokers died, 2 of 12 dogs smoking 3,103 unfiltered cigarettes died, and 24 of 62 dogs smoking 6,129 unfiltered cigarettes died. Common causes of death among smoking dogs included pulmonary infarction, and cor pulmonale. Noninvasive bronchiolo-alveolar tumors were found in the lungs of 12 dogs smoking 518-5,970 cigarettes. Invasive tumors were found in lungs of 4 dogs smoking from 3,928-5,030 cigarettes. Fibrosis and emphysema were found in the lungs of all smoking dogs. It was concluded that smoking cigarettes with an efficient filter will produce less damage to lung parenchyma than smoking unfiltered cigarettes.

- 0974 EFFECT OF CIGARETTE SMOKING ON DOGS: II. PULMONARY NEOPLASMS. (E.) Auerbach, O. (VA Hosp., East Orange, N.J.), E. C. Hammond, D. Kirman and L. Garfinkel. *Arch Environ Hlth* 21(6): 754-768, 1970.

The effect of smoking filtered and unfiltered cigarettes on mortality and pulmonary tumor development was investigated in beagle dogs. Eighty-six dogs trained to smoke through a tracheostoma were divided into 5 experimental groups: nonsmoking controls, smokers of 6,161-6,269 filtered cigarettes, smokers of 1,055-3,195 unfiltered cigarettes, smokers of 518-6,318 unfiltered cigarettes, and smokers of 3,769-5,400 unfiltered cigarettes. By the 875th day after the commencement of smoking, 2 filtered cigarette smokers, and 26 nonfiltered cigarette smokers had died, while none of the nonsmoking controls had died. While noninvasive bronchiolo-alveolar tumors were found in dogs from all 5 groups, invasive tumors were found only among dogs which smoked large numbers (e.g., more than 3500) of unfiltered cigarettes. Early bronchial squamous cell carcinoma was found in 2 dogs, both of which had smoked more than 6000 unfiltered cigarettes. Dogs with tumors in both bronchiolo-alveolar lobes were found in the group smoking unfiltered cigarettes heavily (20% of dogs in this group). Most bronchial tumors were multicentric, and none of the tumors was metastatic. It was concluded that cigarette smoking increases the risk of developing bronchiolo-alveolar tumors in dogs, and that the risk of tumor development is greater in dogs smoking unfiltered cigarettes than in dogs smoking filtered cigarettes.

- 0975 THE RESPIRATORY EFFECTS OF REGULAR CIGARETTE SMOKING IN WOMEN. (E.) Woolf, C. R. (Dept. Med., U. Toronto, Ontario, Canada) and J. T. Suere. *Amer Rev Resp Dis* 103(1):26-37, 1971.

The effect of cigarette smoking on pulmonary function and sputum production in women was investigated. Subjects were 298 normal Canadian women aged 25-54 yr and included 97 nonsmokers, 30 ex-smokers, 24 light (44 cigarettes/wk) smokers, 63 moderate (117 cigarettes/wk) smokers, and 84 heavy (187 cigarettes/wk) smokers. Prevalence of cough, sputum production, wheezing, and dyspnea increased with increased cigarette smoking. Only heavy smokers consistently reported having more than 4 colds/yr. Chest abnormalities were more frequent in smokers than in nonsmokers; abnormalities included decreased darkening of the lung field on fluoroscopy. Sputum specimens, which were more available from smokers than nonsmokers, showed no malignant cells; macrophages were found in equal amounts in sputum from both smokers and nonsmokers. Carbon particles were more frequent in the macrophages from smokers' lungs than in macrophages from the lungs of nonsmokers. Moderate epithelial squamous cell metaplasia and dyskaryosis were found more frequently in the heavy smokers (dyskaryosis occurring in 27% of nonsmokers, 15% of moderate smokers, and 39% of heavy smokers). Columnar cells were distributed similarly in smokers and nonsmokers, while lymphocytes were more frequent in the sputum of smokers than in the sputum of nonsmokers. Smokers had lower values than nonsmokers for forced vital capacity tests, forced expiratory volume in 1 sec tests, arterialized capillary blood oxygen at rest tests, pulmonary diffusing capacity tests, and tests of fractional uptake of carbon monoxide during exercise.

- 0976 SMOKING AND CANCER OF THE LOWER URINARY TRACT. (E.) Cole, P. (Harvard Sch. Publ. Hlth., Boston, Mass.), R. R. Monson, H. Haning and G. H. Friedell. *New Eng J Med* 284(3):129-134, 1971.

The association of cigarette smoking and transitional or squamous-cell carcinoma of the lower urinary tract was investigated in a survey of 470 cancer patients. More than 90% of the patients had bladder tumors. The age-specific incidence data for bladder cancer for males and females indicated that the risk of bladder cancer for men increases at a constant rate throughout life, while the risk for women began to increase after age 60. Male cigarette smokers had a relative risk of bladder cancer of 1.89 compared with nonsmokers and female smokers had a relative risk of 2.00. About 39% of male cases of bladder cancer were related to smoking, and about 29% of female cases were smoking-related. The highest number of bladder cancer cases among smokers occurred in male patients who smoked from $\frac{1}{2}$ -1 $\frac{1}{2}$ packs of cigarettes/day (140 observed cases). In both sexes, the risk of contracting bladder cancer was increased among smokers who inhale deeply. Attributable risks of bladder cancer for smokers increased with age; risks for patients aged 20-59 yr, 60-74 yr, and 75-89 yr being, resp., 10, 60 and 87 cases/100,000 population. None of the excess risk of bladder cancer associated with cigarette smoking was explained by any indirect association with occupational exposure. It appeared likely that incidence rates for bladder cancer among women will increase in the next 10 yr. Pipe and cigar smoking was not associated with a significant risk of bladder cancer.

0977 THE EPIDERMIS AND THE RESPIRATORY TRACT AS BIOASSAY SYSTEMS IN TOBACCO CARCINOGENESIS. (E.) Wynder, E. L. (Amer. Hlth. Found., New York, N.Y.) and D. Hoffmann. *Brit J Cancer* 24(3):574-587, 1970.

The carcinogenic effects of cigarette smoking have been investigated using the mouse epidermis as a bioassay system. The advantages of mouse skin were that it is responsive to tumorigenic substances in small doses, it responds only to carcinogens and not to non-specific physical agents, and it involves squamous epithelium, which must be formed before malignant transformation can take place in the respiratory epithelium. The smoke of 2 cigarettes, containing about 52 mg of moist particulate matter, was applied 3 times/wk to squamous epithelium of mouse skin. This technique has permitted the identification of tumor initiators in the "tar" fraction of tobacco smoke which included benzo(a)pyrene. Tumor "accelerators" have also been detected; these are components which exhibit neither carcinogenic activity nor tumor initiating activity, but which accelerate the activity of complete carcinogens when applied concurrently with them. Such tumor accelerators include trans-4,4'-dichlorostilbene, 5-methylindole, and 9-methylcarbazole. Tumor promoting agents identified by use of the mouse epidermal bioassay system have been found to reside in the weakly acidic (phenolic) and the acidic fractions of the smoke; the specific identity of these agents, however, remains to be determined. Apparently, the tumorigenicity of tobacco smoke "tar" declines significantly when pyrosynthesis of alkylated and non-alkylated polynuclear hydrocarbons is inhibited.

0978 THE EFFECTS OF BETEL-NUT CHEWING ON THE BUCCAL MUCOSA OF 296 INDIANS AND MALAYS IN WEST MALAYSIA: A CLINICAL STUDY. (E.) Chin, C. T. (Dist. Hosp. Kluang, Johore, West Malaysia) and K. W. Lee. *Brit J Cancer* 24(3):427-432, 1970.

The association of betel-nut chewing and changes in the buccal mucosa was investigated in a Malay and Indian population in West Malaysia, where the habit is widespread. The 212 Indians in the study ranged in age from 12-74 yr, and the 84 Malays ranged in age from 25-90 yr; 167 of the Indians incorporated tobacco in their betel-nut quids, while 45 of the Malays substituted gambir for tobacco in their betel-nut quids. Sixty-two percent of tobacco-chewing Indians showed changes in the buccal mucosa; of these changes 40% were designated "leukoplakia" and 23% were designated "preleukoplakia." Only 26% of non-tobacco-chewing Indians showed changes in the buccal mucosa; 9% of these changes were considered to be leukoplakia. Changes in the buccal mucosa were observed in 22% of gambir-chewing Malays, and 11% of these were regarded as leukoplakia and a similar proportion were regarded as preleukoplakia. Among non-gambir-chewing Malays, 25% showed changes, 12% with leukoplakia-like conditions, and 12% with preleukoplakia-like conditions. These results appear to indicate that quids without tobacco are less potent inducers of changes in the

buccal mucosa than quids with tobacco. No dose-effect relationship between changes in the buccal mucosa and light or heavy chewing could be demonstrated.

0979 THE EFFECTS OF BETEL-NUT CHEWING ON THE BUCCAL MUCOSA: A HISTOLOGICAL STUDY. (E.) Lee, K. W. (Inst. Dental Surg., London, England) and C. T. Chin. *Brit J Cancer* 24(3):433-441, 1970.

The histological appearance of leukoplakias from the mouths of West Malaysian betel-nut chewers was examined microscopically. Subjects were Indians and Malays; there were 42 Indians who chewed a quid containing tobacco, and the durations of their chewing habits ranged from 1-50 yr. The remainder of the study population was composed of chewers of quids which did not contain tobacco. An amorphous von Kossa positive layer was seen on the keratin surface in 42 subjects; tobacco was apparently unrelated to this layer. Of 42 tobacco-chewers, 9 showed orthokeratosis, 31 showed parakeratosis, and 12 showed mixed ortho- and parakeratosis. The numbers of non-tobacco-chewers (10 cases) who showed these 3 conditions were resp., 3, 4 and 3. Nine biopsies showed epithelial atypia, all from tobacco-chewing subjects. The average number of mitoses/100 μ length of the basal layer was 0.044 in subjects without leukoplakia and 0.123 in patients with leukoplakia. Long duration of chewing habit seemed to be correlated with relative thinness of buccal epithelium; most chewers whose habit was of 30-40 yr standing had epithelial thicknesses in the 100-250 μ range, while those who had chewed for less than 10 yr were more likely to have epithelia from 450-500 μ in thickness. Eight of the 9 subjects with epithelial atypia had been chewing for more than 10 yr. No relationship between "intensity of habit" (length of time each quid was retained in the mouth of the chewer) and degree of epithelial atrophy was evident. In general, severe histological changes were more likely to be seen in chewers of tobacco-containing quids than in chewers of tobacco-less quids.

0980 TUMORS OF THE URINARY BLADDER: AN ANALYSIS OF THE OCCUPATIONS OF 1030 PATIENTS IN LEEDS, ENGLAND. (E.) Anthony, H. M. (Sch. Med., U. Leeds, England) and G. M. Thomas. *J Nat Cancer Inst* 45(5):879-895, 1970.

The correlation of occupation and development of tumors of the urinary bladder was investigated in a survey of the whole-life occupational histories of 1,030 workers in Leeds, England, with bladder papillomas or carcinomas. Hospital patients with lung cancer and with nonmalignant diseases served as controls. Data on smoking habits of the bladder cancer patients was also compiled, but no clear association between cigarette smoking and the occurrence of bladder tumors could be established. Excesses of bladder tumor patients compared to nonmalignant patients and non-bladder cancer patients were found for workers in the textile and clothing industry, electrical and electronic workers, engineering workers, and service, sport and recreation

workers. Differences in incidence of bladder tumors compared to controls were significant at the 5% level for engineering fitters, engineers, weavers, tailors, and medical workers (mainly nurses). The ratio of textile workers having bladder tumors to controls having bladder tumors was 20:11, and the ratio of clothing workers with tumors to controls with tumors was 19:11. Dye workers were also at risk, with 3 dye workers having bladder cancer. Among clothing workers, tailors and clothes pressers were at especially high risk, the ratio of bladder cancer patients to controls in these 2 occupational categories being 7:0 and 7:2, resp. High risk was usually associated with long-term employment (e.g., employment of more than 20 yr standing). In dye workers, tailors' cutters and hairdressers, tumors appeared at younger ages. The distribution of papillomas and carcinomas in the patients was similar. It was concluded that of the bladder cancer cases observed, the fraction of cancer cases related to occupation may have been in excess of 20%.

- 0981 A CASE OF CHRONIC BERYLLIUM INTOXICATION: PATHOGENIC CONSIDERATIONS AND THE DIAGNOSTIC VALUE OF THE "PATCH TEST". (Fr.) Groetenbriel, C. (Occup. Dis. Med. Council, Brussels, Belgium), W. Van Ganse and J. Oleffe. *Acta Tuberc Pneumol Belg* 61(3-4):363-376, 1970.

A case of chronic beryllium intoxication in a 40-yr-old man who had been exposed to 4 yr of beryllium oxide inhalation while handling fluorescent tubes 15 yr previously is presented. Micronodular opacities in the apical lung region and minor hypertrophic alterations of the right hilar region were found. An immunological mechanism in the pathogenesis of chronic berylliosis and the relationship of beryllium exposure and cancer in humans is discussed. Reference is made to the fact that beryllium containing tobacco is used for smoking in Rhodesia and in Great Britain.

- 0982 ETHMOIDAL CANCER IN WOOD-WORKERS IN THE FURNITURE INDUSTRY. (E.) Macbeth, R. G. (Oxford, England), E. D. Acheson and E. H. Hadfield. *Oto-Rhino-Laryngology* 206:840-842, 1970.

A causal connection between wood dust and adenocarcinoma of the ethmoid sinus was put in evidence. The incidence of ethmoid carcinoma among workers exposed to wood dust in connection with the British furniture manufacturing industry in High Wycombe was investigated. The annual incidence of ethmoid adenocarcinoma in the whole country was 0.00046/1000, while the incidence for this condition among wood workers in the selected town was 0.7/1000. Wood dust deposits in the noses of wood workers were located around the anterior ends of the middle turbinates and in particular on the more roomy side of the nose in the cases of deviated septum.

- 0983 QUALITATIVE CHANGES IN LYMPHOCYTES FOLLOWING BENZENE ABSORPTION. (Ger.) Roth,

L. (2nd Med. Clin. Timisoara, Rumania), P. Turcanu, V. Serban and G. Moise. *Z Ges Inn Med* 25(20):932-935, 1970.

Patients with chronic benzene intoxication in connection with their occupation were investigated for morphological changes in the peripheral blood and the distribution of sinus- and follicular lymphocytes by means of the Stockinger and Kellner staining method. These patients (155) worked in shoe factories where benzene, toluene and acetone were used as solvents, and occasionally the concentration in the atmosphere rose above the permitted threshold. The results of hemograms showed a high incidence of anemias in which slight disturbances in iron metabolism was seen, and which were almost exclusively found in females. In 7 (4.5%) of the tested subjects, massive granulo- and thrombopenias were found. There was also a high incidence of absolute monocytosis (22.5%), and a lesser incidence of changes in the absolute value of lymphocytes (lymphocytosis 7.7%, lymphopenia 5.8%). Large bright lymphoid cells characterized by unusual plasticity of the cytoplasm were observed. Another characteristic feature was the formation of hyperbasophilic lymphocytes. Sixteen cases showed an increase in sinus lymphocytes relative to follicular lymphocytes; of these, 6 showed a complete inversion of the relationship. This inversion of the sinus and follicular lymphocytes was detected in these subjects before any subjective symptoms appeared.

- 0984 BREAST CANCER DURING ORAL CONTRACEPTIVE THERAPY. (E.) Fechner, R. E. (Baylor Coll. Med., Houston, Tex.). *Cancer* 26(6):1204-1211, 1970.

The possibility of an association between the use of oral contraceptives and mammary cancer was explored in 5 women under 35 yr who had been using oral contraceptive pills for periods ranging from 13-60 months. Patients ranged in age from 26-32 yr; all had developed mammary tumors 1.2-3.5 cm in size. In all 5 cases, the invasive neoplasm was a large cell carcinoma of ductal origin; in some cases, remote areas were involved, and metastatic carcinoma involved the axillary lymph nodes in 3 cases. Control cases were composed of mammary cancer cases arising in women who had not used oral contraceptives. Controls included 7 large cell infiltrating ductal carcinomas and 2 intraductal carcinomas without invasion. Four cases showed metastasis to axillary lymph nodes. Controls had a slightly larger average tumor size than test cases, but no gross qualitative differences were seen between the 2 groups.

- 0985 EFFECT OF INTRAUTERINE CONTRACEPTIVE SUTURE ON THE RESPONSE OF RAT UTERUS TO PROLONGED ESTROGEN TREATMENT. (E.) Malaviya, B. (Central Drug Res. Inst., Lucknow, India), J. N. Karkun and A. B. Kar. *Indian J Exp Biol* 8(1):19-21, 1970.

The response of the rat uterus to the insertion of an intrauterine contraceptive suture and to prolonged

rogen administration was investigated. Rats were fitted with a silk suture in 1 uterine horn, and thereafter were given terramycin therapy and i.m. injections of estradiol dipropionate (1 µg/rat/day) for 7 days prior to the insertion in the uterine horn of an intra-uterine contraceptive device (IUCD). After insertion of the IUCD, estradiol dipropionate doses were increased to 2 µg for 3 days, 4 µg for 4 days, and 5 µg for another 136 days. Acid phosphatase activity was markedly greater in the uterine horn containing the IUCD than in the uterine horn containing device (157.5 and 81.8 mg phosphate/100 g/hr in IUCD and control horns, resp.). Glycogen and phospholipid were also increased in the IUCD uterine horn. The endometrium of the control horn was found to be edematous, and exhibited mild polymorphonuclear leukocyte infiltration; cystic hyperplasia was occasionally seen in control horns. Early squamous metaplasia was discernible in places in the control horns. In the uterine horns fitted with IUCD's, polymorphonuclear leukocytic infiltration of the endometrium was more extensive than in control horns, and much of the glandular epithelia and glandular lumina showed massive cystic hyperplasia. Squamous metaplasia of the epithelium was frequent in IUCD-bearing uterine horns. Neoplasia was evident in either control or IUCD uterine horns. Possibly, estrogen treatment and the presence of an IUCD serve to accentuate traumatic reaction in the uterine tissue.

0986 PRESENT STATE OF AUGMENTATION MAMMAPLASTY. (E.) De Cholnoky, T. (Greenwich Hosp., Conn.). *Connecticut Med* 34(11):808-809, 1970.

0987 TRANSPLACENTAL EFFECTS OF 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE AND THE ROLE OF PARTIAL HEPATECTOMY. (Turk). Ozkan, A. U. (Fac. Med., Ankara). *Tip Fak Mec* 23(Supp. 32):1-19, 1970.

0988 CARCINOMA OF THE ESOPHAGUS AFTER CAUSTIC ULCERATION. (Ger.) Schmidt-Baumler, U. (Path. Inst. U. Heidelberg, Germany) and K. Fahr. *Laryng Rhinol Otol* 49(2):827-832, 1970.

0989 ENHANCED WATER SOLUBILITY OF 3,4-BENZOPYRENE BY ADDITION OF 1,2,7-TRIMETHYLXANTHINE (CAFFEINE). 5TH COMMUNICATION. THE ACTION OF CAFFEINE COMPARED TO THE EFFECTS PRODUCED BY OTHER WATER SOLUBLE NITROGEN COMPOUNDS. (Ger.) Eisenbrand, J. (Saar Univ., Saarbrücken, Germany) and K. Baumann. *Deutsch Lebensmittel Rundsch* 66(12):430-432, 1970.

0990 DETERMINATION OF AFLATOXIN B₁ BY TWO DIMENSIONAL THIN-LAYER CHROMATOGRAPHY WITH FLUORODENSITOMETRIC EVALUATION. (Ger.) Schuller, P. L. (Inst. Pub. Hlth., Utrecht, Holland), C. A. H. Verhülsdonk and W. E. Paulsch. *Arzneimittelforschung* 20(10):1517-1520, 1970.

0991 CONTAMINATION OF CEREAL PRODUCTS AND ANIMAL FEED BY AFLATOXIN. (Fr.) Lafont, P. (Lab. Aliment. Toxic., LeVesinet, France) and J. Lafont. *Food Cosmet Toxic* 8(4):403-408, 1970.

See also:

- * (Rev): 0833, 0848, 0850, 0855, 0859, 0879, 0880, 0881
- * (Immun): 1133
- * (Path): 1163
- * (Epid-Biom): 1183, 1185
- * (Misc): 1205

- 0992 FIBROSARCOMA INDUCED BY ALPHA PARTICLE IRRADIATION. (E.) De Estable-Puig, R. F. (Dept. Path., Laval U., Quebec, Canada), J. F. De Estable-Puig and C. Auger. *Virchow Arch Zellpath* 6(4):367-369, 1970.

Production of a fibrosarcoma by subjecting a rat to particulate irradiation is recorded. One rat was exposed to irradiation to the head with α -particles (48 Mev and 1,000 rads/min) produced by a 60 inch cyclotron accelerator. A year after irradiation, a fibrosarcoma was observed on the scalp of the irradiated rat. Microscopically, the tumor cell cytoplasm possessed abundant rough endoplasmic reticulum and well-developed Golgi apparatus. Nuclei were large with irregular invaginations of the nuclear envelope and hypertrophic nucleoli. Many cells had nuclear inclusions in the form of membranes enclosing several sacs or large vesicles filled with a finely granular material of intermediate density.

- 0993 EARLY EFFECTS OF LOCALIZED SINGLE DOSES OF IONIZING RADIATION ON HUMAN BONE MARROW. (E.) Stefani, S. (VA Hosp., Hines, Ill.) and A. Monti. *Acta Radiol* 9(5):449-456, 1970.

The dose effect and effect over time of single doses of ionizing radiation on human bone marrow were investigated. Patients with bronchogenic carcinoma were exposed to daily or weekly doses of 200, 400 or 800 rads in the center of the sternum; radiation was administered at 300 kV at a rate of 48 r/min. The bone marrow of patients exposed to 3 doses of irradiation were examined after 2 days. Cells in the myeloblast-premyelocyte group showed a 25-50% decrease from initial levels; the decrease was more marked at higher doses of radiation. Erythrocytes showed a marked drop which increased with radiation dose, the mean count for these cells reaching a low of 10.8% of the initial count after 800 rads. The relative percentage of lymphocytes rose sharply, the mean being 137.3% for 200 rad and 159.8% for 800 rad. Changes produced by 400 rads of irradiation as a function of time included a relative drop in the myeloblast-premyelocyte group which was evident at 3 hr after exposure, reached its low point after 3 days, and recovered after 6 days. The erythroblasts showed the sharpest relative decrease of any cell component, reaching a 4% of initial cell count at 3 days, and recovering after 6 days. In all cell smears taken 1, 2 and 3 days postirradiation, morphologic abnormalities were observed. Erythroblasts were characterized by an increase in cell size, disruption of the nuclear chromatin pattern, presence of nuclear fragments in the cytoplasm, and double nuclei. No morphologic aberrations were detected in lymphocytes or plasma cells.

- 0994 CLINICAL AND GROSS PATHOLOGICAL FINDINGS IN SWINE RELATIVE TO LATE EFFECTS OF MIXED GAMMA-NEUTRON AND X-IRRADIATION. (E.) Brown, D. G. (Agric. Res. Lab., U. Tennessee, Oak Ridge) and D. F. Johnson. *Radiat Res* 44(2):498-511, 1970.

The effects of mixed gamma-neutron nuclear bomb ir-

radiation and X-irradiation on swine were investigated. Seventy-one swine surviving bomb irradiation in amounts between 15-850 rads were, in some cases, reirradiated with X-rays; pathological and clinical effects were observed for the remainder of the animals' life spans. Irradiated swine weighed on the average 45 kg more than unirradiated controls. Clinical changes were similar in irradiated and control animals except for unilateral atrophy of the musculature in some swine exposed to more than 250 rads. Major causes of death were chronic diseases, the usual clinical syndrome including loss in body wt, debilitation, bacterial infection, and blood changes associated with infections. Mean postirradiation survival times for irradiated swine were 8.3 yr for males and 7 yr for females; survival times for controls were 9 yr for males and 7 yr for females. Mortality rates were higher in irradiated animals through about 7 yr postirradiation, and regression of survival times on dose of irradiation indicated a significant shortening of life of irradiated females. Lesions which were found in significant numbers in irradiated swine and presumably attributable to irradiation were asymmetrical conformation, genital neoplasia usually manifested as leiomyomas of the broad ligaments and uteri, hepatomas, and annular sclerosing adenocarcinomas in the small intestine. Genital tumors appeared earliest in animals exposed to the highest radiation doses. Although genital, hepatic and intestinal tumors developed in all animals, tumors developed earlier in irradiated animals, with controls developing tumors beginning at 9 yr after the beginning of observation and irradiated animals developing tumors beginning at 5-6 yr postirradiation. By 11 yr post-irradiation, 80% of female swine had developed uterine tumors.

- 0995 CARCINOMA OF THE HYPOPHARYNX AFTER IRRADIATION OF THE NECK REGION FOR TUBERCULOSIS OF THE LYMPH NODES. (Ger.) Heilmann, H. P. (Mad. Radiol. Inst., U. Tubingen, Germany). *Strahlentherapie* 140(4):388-391, 1970.

A squamous epithelial carcinoma of the hypopharynx developed in a 69-yr-old woman 50 yr after exposure to roentgen therapy for lymph node tuberculosis in the neck region. The dose monitoring instrument used in 1920 expressed exposure dosages in empirical units which could not be converted to current units. The latency periods for development of malignant tumors through radiation exposure vary in the literature from 3 to 47 yr, with the latency period increasing with lower irradiation dosages.

- 0996 A CASE OF LATE SILICOSIS WITH PLEURAL MESOTHELIOMA. (Fr.) Thzolov, C. (Sofia, Bulgaria) and K. Kolev. *Acta Tuberc Pneumol Belg* 61(3-4):354-362, 1970.

A case of silicosis developed after 14 yr of latency in a 59-yr-old man who spent 10 yr in an uranium mine and was exposed to silicotic dusts and radon radiation is presented. The primary coniotic condition was associated with a later pleural mesothelioma with considerable cellular polymorphism

with the clinical appearance of a lung cancer. Reference is made to the increasing incidence of lung cancer (42%, according to the author's experience) in silicotic patients. The relationship between silicosis and lung cancer is still uncertain. Silicosis may create the favorable conditions for the development of pulmonary neoplasia by triggering the development of pleural mesothelioma in conditions of excessive exposure to pathogenic radiation.

7 ANALYSIS OF ETIOLOGICAL FACTORS OF SQUAMOUS CELL SKIN CANCER OF DIFFERENT LOCATIONS: THE ARM AND THE HAND. (E.) Swanbeck, G. Karolinska Hosp., Stockholm, Sweden) and L. Lästrom. *Acta Dermatovener* 50(5):350-354, 1970.

The distribution of squamous cell carcinoma of the arm and hand was investigated in the Swedish population from reported cases during the period 1958-1965. Of 129 cases of squamous cell carcinoma of the skin on the hand, most cases involved the backs of the hands; 96 of the cases were men and 33 were women. For both sexes the incidence of skin cancer on the hand reached a peak between the ages of 70 and 80 yr (30 male cases and 8 female cases). Specific etiological factors associated with skin cancer on the hands were burn injury (3 cases), X-ray treatment (2 cases), mechanical injury (4 cases) and eczema (3 cases). The fact that more cases of squamous cell skin cancer occurred in outdoor workers than in any other occupational group (40 cases) may indicate that exposure to sunlight is an etiological factor for this condition. Eight cases of skin cancer on the hand had metastasized, 3 of them to the lymph nodes. Cancer of the skin on the arms occurred in 25 cases, of which 11 were men and 14 were women. Age peaks for this condition fell at 55 yr for women and at 65-70 yr for men. No correlation with outdoor work was found for squamous cell skin cancer of the arm; metastases occurred in 11 cases.

98 OCCURRENCE OF ONCOGENOUS X-RAY SUSCEPTIBILITY IN *DROSOPHILA MELANOGASTER* ZYGOTES. (E.) Ghelelovitch, S. (Pasteur Lab., Inst. Radium, Paris, France). *Int J Radiat Biol* 18(4):331-354, 1970.

Specimens of the *cltu* strain of *Drosophila melanogaster* were used to investigate whether irradiation of gametes or irradiation of the fertilized ovum determines the development of tumors in the respective progeny. Males and virgin female flies were exposed to 600 r, 900 r or 1200 r of X-irradiation. Progenies from irradiated females crossed with irradiated males, from irradiated females crossed with nonirradiated males or from nonirradiated females crossed with irradiated males revealed no differences in tumor incidence with respect to progenies from nonirradiated parent gametes. The tumor incidence in progenies from females exposed to 900 r after insemination was compared to 26% in controls, revealing stimulation of tumorigenesis in specimens developed from irradiated zygotes. The environmental con-

ditions within the maternal organism seemed to have no protective effects against X-ray exposure. The lack of tumorigenic effects in progenies originating from male and female gametes irradiated before their fusion and the appearance of such effects following the irradiation of zygotes seem to indicate that the fertilization of the ovum may constitute the event determining the tumor susceptibility to X-irradiation.

0999 STIMULATION OF LEUKEMOGENESIS BY FRACTIONATED X-RAY RADIATION; INHIBITORY ACTION OF HYDROCORTISONE. (Fr.) Mistry, P. B. (Inst. Radium, Paris, France), P. Monnot and J. F. Duplan. *C R Soc Biol* 164(4):697-700, 1970.

The effect of hydrocortisone on AKR or C57BL mice exposed to intermittent irradiation was compared to effects produced by treatment with isogenous bone marrow cells. The animals (AKR and C57BL mice) were irradiated 4 times within 1 wk, the first irradiation being administered at a mean age of 40 days. The injection of hemopoietic cells was administered 24 hr after the final irradiation (8×10^6 to 12×10^7 nucleated cells from isogenic bone marrow). The animals treated with hydrocortisone received 0.5 mg 3 times a week for 3 wk (AKR mice) and for 4 wk (C57BL), commencing immediately following the last irradiation. The incidence and latency of leukemias in the normal AKR mice was 90% at the age of 323 days. After fractionated radiation, all died of leukemia at the mean age of 205 days. Under treatment of hydrocortisone, the incidence of leukemias was 95% and latency was 288 days. In the C57BL mice, fractionated irradiation increased the incidence from 2.5 to 81% and decreased the latency from 612 to 261 days. Cortisone administration caused an incidence of 39% and latency of 297 days. The incidence of leukemia decreased to 10% and the latency period increased to 528 days after treatment with isogenous bone marrow cells. This specific treatment produced better results in C57BL mice than in AKR mice. Hydrocortisone exhibited inhibitory effects on leukemogenesis in both investigated mouse lines.

1000 BONE CANCERS INDUCED BY ^{224}Ra (Th X) IN CHILDREN AND ADULTS. (E.) Spiess, H. (Child. Polyclin., U. Munich, Germany) and C. W. Mays. *Health Phys* 19(6):713-729, 1970.

The induction of bone sarcomas by therapeutic exposure to ^{224}Ra for the treatment of tuberculosis, ankylosing spondylitis, and other diseases was investigated. Subjects included 217 children and 708 adults; the average skeletal dose of radium was 140 $\mu\text{C}/1000$ esE, which amounted to an average dose in rads to the marrow-free skeleton of 0.6 rads for children aged 1-15 yr, 0.4 rads for those aged 16-20 yr, and 0.2 rads for adults. Forty-nine patients developed bone sarcomas; the lowest skeletal dose of radium among patients developing tumors was 90 rads. Fifteen percent of children and 1.4% of adults developed bone sarcomas, yielding incidence rates for tumor development/100 rads of 1.38% for children and 0.69% for adults. In 19 cases, 5-11 yr elapsed be-

tween radium exposure and appearance of sarcomas. Radium induction of sarcomas was equally efficient in males and females and in patients with and without bone disease at the time of radiation. Twenty-one soft-tissue tumors developed in the study population, but none was thought to be related to radium exposure.

- 1001 ACUTE RADIATION INJURY IN NEONATALLY THYMECTOMIZED GERM-FREE MICE: HEMATOPOIETIC AND MORPHOLOGIC CONSEQUENCES. (E.) Doughty, W. E. (Sch. Med. U. New Mexico, Albuquerque), R. E. Anderson, J. L. Howarth and S. Tokuda. *Arch Path* 91(2):119-126, 1971.

The hematologic and morphologic consequence of a single whole body exposure to 700 rads of cobalt 60 γ -rays in neonatally thymectomized germ-free mice and the role of the thymic-dependent lymphoid reserve in subsequent recovery were studied. At 6 wk of age, 64 intact and 112 thymectomized mice were exposed to γ -irradiation; on days 4, 8, 12, 20, 24, 28, 32, 40 and 150 postirradiation, 4 mice from each group were bled and sections were prepared from their organs. Four intact and 4 thymectomized non-irradiated mice were similarly treated at 6 and 27 wk of age as controls. The cumulative mortality was 9.3% and 18.3% in the intact-irradiated and thymectomized-irradiated groups, resp. Following radiation, total leukocytes dropped to less than 500/mm³ in both groups, recovered, and exceeded control levels by 20-24 days postexposure; this peak was followed by another decrease and recovery cycle peaking at day 40. The absolute lymphocyte count variation was directly related to the total leukocyte count; mean hematocrit values decreased transiently postirradiation. Spleen wt decreased to half of control values at 10 day postirradiation and more than doubled at 20-24 days following exposure before returning to control values at 30 days. Hematopoietic colony forming unit proliferation in spleen and bone marrow more or less followed the changes in spleen wt. The thymus gland of the intact irradiated mice underwent hyperplasia initially, but by 20 days postexposure had less cellularity than control animals. Microscopic abnormalities were not found in the heart, lung, gonads, and liver of either group. The hematological response to radiation injury appears to be modified by thymectomy, favoring the nonoperated over the thymectomized mice.

- 1002 CHROMOSOME ABERRATIONS INDUCED BY X-RAY THERAPY AND MYXOVIRUS INFECTION IN HUMAN PERIPHERAL LEUKOCYTES. (E.) Stenman, S. (3rd Dept. Path., U. Helsinki, Finland), S. Nordling, L. R. Holsto and E. Saksela. *Mutat Res* 10(6):607-616, 1970.

The induction of chromosome aberrations by X-irradiation and myxovirus infection was investigated in phytohemagglutinin-stimulated lymphocytes from 29 women who had undergone radical surgery for cancer of the breast. Patients were given 250 kV of X-irradiation in 4 areas near the left breast and shoulder. Correlations between X-ray dose and chromosome aberration for these patients' lympho-

cytes, and for lymphocytes from irradiated patients with myxovirus infection were studied. Dicentric and rings increased in incidence as X-irradiation doses increased, with the number of aberrations/cell approaching 0.2 as irradiation doses increased from 1000-10,000 rads; the equation for the yield of dicentric and rings was $y = 0.0086 + 1.53 (\pm 0.15) \times 10^{-5} D$, where D is equal to the accumulated skin dose of X-ray in rads. The incidence of fragments/cell was similar, and corresponded to the equation $y = 0.022 + 1.68 (\pm 0.17) \times 10^{-5} D$. The percentage of all damaged cells peaked at 22% between 6000-7000 rads, and dwindled at doses exceeding this. Irradiation did not affect the numbers of aneuploid cells, nor did it markedly decrease the percentage of chromatid-damaged cells. Lymphocytes from irradiated patients were infected with Newcastle disease virus, Sendai virus, measles virus, and mumps virus, and controls were given normal allantoic fluid. The frequency of chromatid-type aberrations in controls increased after irradiation, while none of the viruses caused significant increases. Virus treatment did not significantly affect the frequency of chromosome-type aberrations. Radiation therapy increased the frequency of aneuploid cells from 5% before therapy to 15% at the end of therapy for all virus-infected cells; percentages of tetraploid cells increased with therapy from 0.4-0.6%. In all dose ranges of X-irradiation, the distribution of cells with chromosome breaks deviated from a Poisson distribution unless the number of undamaged cells present in excess was omitted from calculations. Almost 30% of circulating lymphocytes appear to have been exposed to irradiation by the area-irradiation method used.

- 1003 SPECULATED RISK TO BONE AND LIVER FROM ²³⁹Pu. (E.) Mays, C. W. (Radiobiol. Div. U. Utah, Salt Lake City), G. N. Taylor, W. S. S. Jee and T. F. Dougherty. *Health Phys* 19(5):601-610, 1970.

The risk of developing bone and liver cancer following exposure to ²³⁹plutonium was estimated speculatively on 3 models of the incidence of tumor development extrapolated from available human and animal dose-response data. The threshold model of risk of bone and liver tumors was developed from data on tumor incidence in humans exposed to radium, while the dose-rate model and the lifespan dose model were developed from data on tumor incidence in dogs exposed to plutonium. The acceptable body burden of ²³⁹plutonium in radiation workers is 0.04 μ C. Plutonium reaching the circulatory system from occupational exposure is deposited approximately equally in bone and liver. Fifty-yr doses to man for a constant dose of 0.02 μ C of ²³⁹plutonium in bone and liver were calculated as 14 and 57 rads. From these doses the probability of radiation-induced tumors in the liver and bone with the threshold model are 0% for both bone and liver. The probability of tumor induction in these organs with the dose-rate model are 1% for bone and 2% for liver. The probability of tumor development following ²³⁹plutonium exposure for bone and liver with the lifespan model are 5% and 10%, resp. Hazards to the lung from inhaled

autonium and hazards for tumorigenesis at exposed wound-puncture sites were not estimated. The risks calculated referred to adult ^{239}Pu exposure only.

- 004 DIFFUSE PLEURAL MESOTHELIOMA: A CLINICAL AND PATHOLOGICAL STUDY. (E.) Roberts, G. (Southern Gen. Hosp., Glasgow, Scotland). *Brit Dis Chest* 64(4):201-211, 1970.

Clinical and pathological features of cases of diffuse pleural mesothelioma were investigated in a Glasgow hospital. The hospital served a population which was mainly employed in shipyards, and which incurred a high risk of asbestos exposure. Over 18 yr, 20 cases of diffuse pleural mesothelioma were found among 6406 necropsies, with 15 cases reported from the second 9-yr period. Of these cases, 19 were middle-aged or elderly patients, and 16 were men. Six of the male patients had some occupational connection with the shipbuilding industry. In 18 cases, presenting symptoms included dyspnea and chest pain; 15 cases showed evidence of pleural effusion at the time of admittance to the hospital. Seventeen of the patients died within 12 months of the onset of symptoms. In all cases, pleural involvement by the tumor was extensive, partially or completely obliterating the pleural cavity. In 16 cases, the mesothelioma was unilateral, the lung parenchyma was infiltrated. The mediastinal lymph nodes were infiltrated in 9 cases, the pericardium in 6 cases; spread outside the thorax was found in 6 cases. Distant metastases were not common; 11 tumors showed an epithelial pattern and 6 were mesenchymal. Asbestos bodies were found in the lungs of 18 of the cases; there was histological evidence of asbestosis in 13 cases.

- 005 CHROMOSOME ABERRATIONS IN SWINE LEUKOCYTES AFTER *IN VIVO* OR *IN VITRO* EXPOSURE TO 14 MeV NEUTRONS. (E.) McFee, A. F. (U. Tennessee-Atomic Energy Comm. Agric. Res. Lab., Oak Ridge), M. W. Banner and M. N. Sherrill. *Radiat Res* 44(2):512-522, 1970.

The efficacy of irradiation with MeV neutrons in causing chromosome aberrations in pig leukocytes irradiated *in vivo* and *in vitro* was investigated. Female pigs, averaging 206 pounds in wt, were subjected to whole-body neutron irradiation, and venous blood samples were irradiated simultaneously. Leukocyte cultures were established from control, *in vivo*-irradiated pigs and *in vitro*-irradiated cells, and chromosome aberrations, including deletions, dicentric, rings, and breaks, were examined in each culture. Neutron irradiation was more effective in producing chromosome breaks in *in vitro*-irradiated cells than in *in vivo*-irradiated cells. Breaks in *in vitro*-irradiated cultures averaged 2.4 total breaks/cell at 200 rads, while at the same dose *in vivo*-irradiated cells averaged 0.7 breaks/cell. At 300 rads, chromosome deletions averaged 1.4/cell in *in vitro*-irradiated cells, and 0.9 in *in vivo*-irradiated cells. At 350 rads, dicentric and rings averaged 0.5/cell in *in vitro*-irradiated cells and 0.2 in *in vivo*-irradiated cells. These findings

permit the derivation of formulae for the prediction of chromosome aberrations in *in vitro*- and *in vivo*-irradiated cells. The prediction formulas are, for *in vitro* breaks/cell, $Y = 0.00068D + 0.47$; for *in vivo* breaks/cell, $Y = 0.0068D - 0.539$, where D represents the neutron dose administered to a blood sample or measured in air at the recipient animal's midline.

- 1006 NATURAL THORIUM IN HUMAN BONE. (E.) Lucas, H. F. Jr. (Argonne Natl. Lab., Ill.), D. N. Edgington and F. Markun. *Health Phys* 19(6):739-742, 1970.

The thorium content in the bone matter of normal humans was determined in a survey of the ^{232}Th content in the rib bones from 38 individuals. The concentrations of ^{232}Th ranged from less than 0.1-72 ng/g bone ash. The high figure was markedly higher than the next highest value for ^{232}Th concentration, 42.4 ng/g, and was recorded from a man who had had a 40-yr occupational exposure to thorium dust. Thorium concentrations increased with age, with concentrations of 2.5 ng/g for 20-yr-olds, compared to concentrations of 10 ng/g for 70-yr-olds. The increase of ^{232}Th concentration with age fitted the equation: $Y = (0.16 \pm 0.02)T$, where Y = the ^{232}Th concentration in ng/g bone ash and T = the age in yr. Smokers were thought to have increased ^{232}Th concentrations compared to nonsmokers.

- 1007 HISTOPATHOLOGY OF LATE LOCAL RADIOLESIONS IN THE GOAT BRAIN. (E.) Andersson, B. (Gustav Werner Inst., Uppsala, Sweden), B. Larsson, L. Leksell, W. Mair, B. Rexed, P. Sourander and J. Wennerstrand. *Acta Radiol* 9(5):385-394, 1970.

Histopathological examinations were made on deep-brain lesions produced in goats by cross-fire irradiation with 185 MeV proton-beams. Adult goats were exposed to proton irradiation in doses of 15,000 rads (1 animal) or 20,000 rads (5 animals) and killed 1½-4 yr later. Lesions were located in the thalamus, optic chiasma, optic tract, pallidum and internal capsule. Following the acute degeneration produced by irradiation, lesions appeared to progress in 3 phases. At 3-4 wk post-irradiation, necrosis and inflammatory reactions were observed; thereafter, progress of the lesions was characterized by resorption of cellular debris and by the beginning of glial scar formation. This phase was marked by astrocyte proliferation around the necrotic area, and by occasional giant cells, formation of new capillaries, and round cell proliferation. The late stage was marked by prominent glial scar formation, lesions showing no inflammatory reaction, no giant cells, no teleangiectasis, and no hemorrhage. No evidence of cellular elements resembling neoplastic development was found, and it appeared that no untoward late developments followed proton-irradiation in the goat brain.

- 1008 CHROMOSOME CONSTITUTION AND ITS BEARING ON THE CHROMOSOMAL RADIOSENSITIVITY IN MAN. (E.) Sasaki, M. S. (Inst. Med. Genet., Tokyo,

Japan), A. Tonomura and S. Matsubara. *Mutat Res* 10(6):617-633, 1970.

The relation between chromosome constitution and chromosomal radiosensitivity of lymphocytes was studied by analyzing the types and frequencies of radiation-induced (γ -rays, 160 r) chromosome aberrations in blood samples from 49 patients with various types of inborn chromosome abnormalities. Chromosomal radiosensitivity was consistently higher in trisomic cells (whole or part of a chromosome) than in normal cells but was not affected by monosomic conditions, reciprocal translocation, or inversion. An age dependency for radiosensitivity was observed in the level of exchange aberrations which were elevated in the neonatal stage but dropped to the expected level of adults within the first 1 or 2 years, but the level of deletions was not dependent on either chromosomal constitution or the age of the subject. The increased chromosomal radiosensitivity in trisomic cells and the susceptibility of the affected subjects to neoplasia suggest that trisomic cells are particularly cancer-prone and that the illegitimate repair of chromosome damage (intrinsic to trisomic cells) may be a common pathway in carcinogenesis.

1009 THE ULTRASTRUCTURE OF THE LUNG OF MICE EXPOSED TO A SUPRA-LETHAL DOSE OF IONIZING RADIATION ON THE THORAX. (E.) Maisin, J. R. (Dept. Radiobiol., C. E. N./S. C. K., Mol, Belgium). *Radiat Res* 44(2):545-564, 1970.

Electron microscope examinations were conducted on the lungs of mice which had been exposed to supra-lethal doses of ionizing radiation to the thorax. Mice were given doses of 2000 rads of X-irradiation to the whole chest or to the right hemithorax, and ultrastructural studies were carried out 0-15 months thereafter. Three to 6 hr after exposure, lesions were limited to certain foci; however, all types of lung cells showed changes, and the interstitial tissue was dissociated by edema. At this early stage, the cytoplasm of granular pneumocytes showed dilation of the endoplasmic reticulum. Most mice irradiated at the whole chest died between 2-7 months after irradiation; the lungs showed accumulation of myelin-like figures, cell debris, and fibrin-like material in the lumen of the alveoli. Increases in size and number of granular pneumocytes, severe lesions in the capillaries, and an increase in the number of macrophages, neutrophilic leukocytes and plasmocytes also characterized this intermediate stage. Nuclei of granular pneumocytes at this stage were hypertrophied and irregular. Collagen fibers and elastic fibers, however, were only slightly more abundant during the intermediate stage than normally. Mice which survived the intermediate phase showed extensive sclerosis and hyalinization of the alveolar septa associated with lesions in the capillaries. In this final or chronic stage, granular pneumocytes appeared to be normal but were largely diminished in number. Lesions in the capillaries seemed to play an important role in the development of ultrastructural changes in the lung epithelium and in interstitial tissue; however, it is difficult

to assess the contributions to the total picture of ultrastructural change of direct radiation damage to cells and of indirect damage by impaired blood circulation.

1010 BREAST CANCER AND CALCIFIED FATTY TISSUE TRANSPLANTS AFTER PLASTIC SURGERY FOR BREAST ENLARGEMENT. (Ger.) Hermanutz, D. (Radiol. Clin. U. Bonn, Germany) and R. Müller. *Fortschr Roentgenstr* 113(4):530-533, 1970.

Calcium deposits are often seen in the breast both with malignant and benign tumors and may be detected by radiological technique. Malignancy is characterized by a "granular" appearance of such calcification and is found in about 1/3 of the cases. The case of a 30-yr-old patient with palpable nodes in the right breast and a well-defined node in the right axilla, is described. Microcalcifications were observed in X-rays films; additional evidence of carcinoma was the presence of dilated vessels in the tumor area, a characteristic of this type of carcinoma. Histologically, the tissue revealed a predominantly solid, partially adenoid carcinoma in sections of the lactiferous ducts and fine granular calcified foci of necrotic cell bands in the tumor. At the age of 24 yr the patient had received subcutaneous fat tissue transplantation in both breasts to correct a hypoplasia. The mother and sister of this patient had died of carcinoma, the former of mammary carcinoma. The question whether plastic breast surgery would increase the incidence of mammary gland carcinoma is raised.

1011 PROLIFERATIVE ACTIVITY OF THE STEM CELLS IN THE BONE-MARROW OF MICE AFTER SINGLE AND MULTIPLE IRRADIATIONS: TOTAL-OR PARTIAL-BODY EXPOSURE. (E.) Croizat, H. (Inst. Gustave-Roussy, Villejuif, France), E. Frindel and M. Tubiana. *Int J Radiat Biol* 18(4):347-358, 1970.

Female mice were given single doses of 150 rads of X-irradiation to the whole body (40 mice) or a similar dose with the right leg shielded (249 mice); mice in another group were subjected to 1000 rads of whole-body irradiation. In the iterated X-irradiation experiments, 60 mice were given subtotal irradiation daily (150 rads for 2-11 irradiation sessions in total); a comparison group was given 1000 rads of whole-body irradiation. Numbers of stem cells in the bone marrow of irradiated mice were determined, as were the proportions of stem cells synthesizing DNA. Mice receiving a single dose of radiation showed a transient decrease of stem cells in the shielded marrow followed by a rise to 125% of the initial number of stem cells from 7-48 hr after irradiation. The proportion of stem cells synthesizing DNA remained at 50% of normal 24 hr after irradiation. In irradiated leg bone marrow, the number of stem cells decreased rapidly to 50% of control and remained at this level for the next 24 hr. The proportion of cells in DNA synthesis increased sharply immediately after irradiation, then fell off to 12% of controls before rising again to 50% at 24 hr. After whole body

radiation, the number of stem cells fell to 55% of normal and changed little thereafter. By 24 hr post-radiation the proportion of stem cells in DNA synthesis was slightly higher than unirradiated controls. In repeatedly irradiated mice the number of stem cells in the marrow of the protected leg decreased steadily and reached 10% of normal values at the end of the course of irradiation. In repeatedly irradiated areas the number of stem cells dropped during the first days to 0.5% of the initial value and increased slowly thereafter to 1.5% of initial values at the end of the irradiation course. In protected marrow after the second irradiation session the number of cells synthesizing DNA was twice the initial number, later decreasing to 2% of initial numbers. However, the proportion of cells in DNA synthesis remained higher than in controls. The depletion of protected bone marrow stem cells following irradiation and their subsequent recovery is apparently due to migrating hematopoietic cells between irradiated cells and protected regions.

1012 DISTRIBUTION OF ^{239}Pu IN THE BONE MARROW AND ON THE ENDOSTEAL SURFACE OF THE FEMUR OF ADULT RABBITS FOLLOWING INJECTION OF $^{239}\text{Pu}(\text{NO}_3)_4$. (E.) Bleaney, B. (Churchill Hosp., Oxford, England) and J. Vaughan. *Brit J Radiol* 44(517):67-73, 1971.

The distribution in bone tissue of plutonium following a dose of $^{239}\text{Pu}(\text{NO}_3)_4$ was studied in rabbits. Rabbits were given either 2.62, 1.24, 1.25, or 2.5 $\mu\text{C/kg}$ of $^{239}\text{Pu}(\text{NO}_3)_4$. In the 1.25 μC dosage group, the dose was administered i.v., while in other dosage groups the dose was administered i.m. At all dose levels, the distribution of plutonium given i.m. was diffuse for the first 35 days postinjection; aggregates of plutonium began to appear at 112 days. In rabbits given 1.24 μC doses, the plutonium level at the injection site dropped more rapidly than in the group given 2.62 μC , and, as a consequence, radiation doses in the marrow were higher in shorter times in the lower dosage group. Estimation of the amount of plutonium in cells at the surface of the marrow showed that the amount increased by a factor of 5 between 8-112 days after i.m. injection. More plutonium was found in the endosteal cells after i.m. injection of 2.5 μC (50% of the total plutonium was retained in the endosteal area in the i.m. group as opposed to 30-44% in the i.v. groups). In cells of the endosteal surface, 40% of the total plutonium was present in the endosteal cells themselves, and 60% was located on the mineral or matrix of the bone surface free of cells. Plutonium was also found in the osteogenic cells themselves, a finding which may account for the virulent carcinogenicity of plutonium.

1013 TOXICITY OF INHALED ^{90}Sr FUSED CLAY IN BEAGLE DOGS: I. (E.) Barnes, J. E. (no affil), B. B. Boecker, C. H. Hobbs, R. K. Jones, G. M. Kanapilly, J. L. Mauderly, R. O. McClellan and J. A. Pickrell. *Fission Products Inhalation Program Annual Report* 1969-1970: 188-196, 1970.

The retention of Sr^{90} fused clay in the body of beagle dogs 8-256 days after inhalation of aerosol Sr^{90} fused clay was investigated. Initial lung burdens of Sr^{90} ranged from 30-680 $\mu\text{C/kg}$. Sixty-

four percent of the aerosol inhaled was deposited in the dog; of that amount deposited in the dogs' body, 57% was found in the pulmonary region. The percentage of Sr^{90} retained in the bodies of dogs declined with time; by the end of the first day after inhalation, percentages of retained Sr^{90} dropped 100-40% thereafter leveling off at 30% and 28% retention by days 180 and 265, resp. The rapid initial loss was thought to represent the rapid clearance of the upper respiratory tract which occurred with a half-time of about 0.35 days. The gradual phase of decline in retained Sr^{90} is consistent with a half-life of 420 days for Sr^{90} , with a biological half-life of 440 days. By 512 days after inhalation, 89% of the retained Sr^{90} was located in the lungs, 6% in the skeleton and 3% in the tracheobronchial lymph nodes. Sr^{90} retention in other organs was negligible; however, activity in the liver comprised a small percentage of the total body burden of Sr^{90} until 256 days after inhalation. Although no dogs died of Sr^{90} inhalation, those dogs given the largest doses showed signs of radiation pneumonitis when their cumulative radiation doses reached 40,000-47,000 rads in the lungs.

1014 TOXICITY OF INHALED $^{90}\text{SrCl}_2$ IN BEAGLE DOGS: IV. (E.) Boecker, B. B. (no affil), T. L. Chiffelle, C. H. Hobbs, R. K. Jones, R. O. McClellan, J. A. Pickrell and H. C. Redman. *Fission Product Inhalation Program Annual Report* 1969-1970 :123-127, 1970.

The toxic and carcinogenic effects of ^{90}Sr , inhaled as an aerosol of $^{90}\text{SrCl}_2$ by beagle dogs, was investigated. At 14 days after inhalation of the compound, mean body burdens of ^{90}Sr for the dogs ranged from 1.4-75 μC of $^{90}\text{Sr/kg}$. Dogs with 14-day body burdens of ^{90}Sr of 50-100 $\mu\text{C/kg}$ had markedly shorter survival periods than dogs with lower body burdens. Nineteen dogs died or were killed between 585-1787 days postinhalation; of these dogs, 7 had angiosarcomas, 3 had fibrosarcomas, 5 had osteosarcomas, 1 had osteochondrosarcoma, 1 had osteochondrofibrosarcoma, 1 had leukemia, 1 had an epileptic seizure, and 1 had cerebellar hemorrhage. The cumulative radiation doses to the skeletons of the dogs in this group at death from the inhaled ^{90}Sr ranged from 4000-22,000 rads.

1015 TOXICITY OF INHALED $^{144}\text{CeCl}_3$ IN BEAGLE DOGS: IV. (E.) Boecker, B. B. (no affil), S. A. Benjamin, T. L. Chiffelle, R. K. Jones, C. H. Hobbs, R. O. McClellan, J. A. Pickrell and H. C. Redman. *Fission Products Inhalation Program Annual Report* 1969-1970 :128-136, 1970.

The toxic effects of ^{144}Ce , inhaled as $^{144}\text{CeCl}_3$, was investigated in beagle dogs. Fifty-five dogs which inhaled the compound were placed in a longevity study for lifelong observations. The ^{144}Ce burden of these dogs at 14 days after inhaling $^{144}\text{CeCl}_3$ ranged from 0 $\mu\text{C/kg}$ for controls not inhaling the compound to a high of 230 $\mu\text{C/kg}$. It was found that inhaled ^{144}Ce deposited in the lung was rapidly transferred to liver and skeleton. By 450 days after inhalation,

the lung contained less than 1% of the initial lung burden of ^{144}Ce , while the liver and skeleton contained 50% and 30%, resp., of the initial lung burden. Seventeen dogs from the 120 and 230 $\mu\text{C/kg}$ ^{144}Ce body burden groups died by 510 days after inhalation. Of these, 3 had hepatic necrosis, 1 had pulmonary fibrosis, 1 had marrow aplasia and 2 had tumors. One of the tumor-bearing dogs had an osteogenic sarcoma, and 1 had squamous cell carcinoma of the maxilla and a small papillary adenoma of the lung.

1016 RADIOPATHOLOGY OF AMERICUM 241: I. DISTRIBUTION OF AMERICUM IN ADULT MICE. (E.)
Hammarstrom, L. (Roy. Vetr. Coll., Stockholm, Sweden) and A. Nilsson. *Acta Radiol* 9(5):433-442, 1970.

See also:

- * (Rev): 0835, 0836, 0845, 0855, 0861, 0874
- * (Chem): 0986
- * (Immun): 1136
- * (Epid-Biom): 1172

- 7 VIRUS-LIKE PARTICLES IN RHABDOMYOSARCOMA WITH EPIDERMODYSPLASIA VERRUCIFORMIS. (E.) Imoto, T. (Fukayama Natl. Hosp., Hiroshima, Japan), Y. Yabe and S. Ohmori. *Dermatologica* 141:309-314, 1970.

Rhabdomyosarcoma located on the chest wall of a 4-yr-old man who also had squamous cell carcinoma of the leg and metastasis to the right inguinal lymph node was found to contain virus-like particles. The rhabdomyosarcoma exhibited epidermodysplasia verruciformis. Under the light microscope, the tumor showed pleomorphism, and numerous giant cells, often having bizarre nuclei and vacuolated cytoplasm. Under the electron microscope, virus-like particles were demonstrated; the particles ranged 90-110 nm in diameter, with nuclei of about 50 nm. The particles were apparently C-type, and appeared in both cytoplasm and extracellular spaces. Four rhabdomyosarcomas without epidermodysplasia verruciformis were examined and found to lack virus-like particles.

- 8 VIRUS-LIKE PARTICLES IN CULTURED HUMAN GLIOMA. (E.) Tani, E. (Kyoto U. Med. Sch., Japan), J. Takeuchi and T. Ametani. *Acta Neuropath* 16(3):266-270, 1970.

Segments of the tumor mass cultured for 30 days and surgical specimens from a patient with glioma were examined by light and electron microscopy. The tumor cells exhibited a pleomorphism with elongated nuclei and scant cytoplasm. Nucleoli contained annular components and glycogen particles were scattered throughout the cytoplasm. Round virus-like particles (100-110 mμ in diameter) were observed in the extracellular site of the cultured tumor cells. The particles had a homogeneous dense core (60-70 mμ in diameter) and were surrounded by a limiting membrane with no spikes or spicules. The virus-like particles suggested a mature type C virus although budding at the cell membrane (characteristic of immature type C virus) was not observed.

- 9 VIRUS-INDUCED POLYKARYOCYTOSIS AND THE MECHANISM OF CELL FUSION. (E.). Poste, L. (Roy. Postgrad. Med. Sch., London, England). *Advances Virus Res* 16:303-356, 1970.

Aspects of the process of polykaryocytosis and cell fusion are discussed with emphasis placed on viral-induced phenomenon. Time-lapse cinematographic studies, electron microscopy, cell marker and nuclear count techniques and studies of single cells are given as evidence of viral polykaryocytes being formed by cell fusion. Differences in the ability of cells to fuse following virus infection are striking with a higher fusion capacity exhibited by malignant and established cell lines and "young" cells and is ultimately dependent upon the genetic constitution of the virus modified by culture media and techniques. Viruses which induce cell fusion cause a reduction in the thickness of the cell coat to below 35 Å by release of lysosomal

hydrolases, a process which can be inhibited by stabilizing agents which also prevent cell fusion. The membrane fusion process is energy-dependent, involving fundamental reorganization of membrane structure. There is little detailed knowledge of the biochemical and molecular events involved in the process. (334 references)

- 1020 EFFECT OF NEOCARZINOSTATIN ON THE CULTURED BURKITT LYMPHOMA CELLS, WITH PARTICULAR REFERENCE TO THE ENHANCEMENT OF PRODUCTION OF EPSTEIN-BARR VIRUS. (E.) Sairenji, T. (Sch. Dent., Tohoku U., Sendai, Japan), J. Yamaguchi, S. Katagiri and Y. Hinuma. *Cann* 61(5):451-460, 1970.

The relationship between Epstein-Barr virus synthesis and the growth of host cells harboring the virus was studied. Neocarzinostatin, in amounts of 1 or 10 μg/ml, was added to cultures of Burkitt lymphoma cells, and the effect on cell division and on the presence and activity of virus in the cells was observed. Treatment with 1 μg/ml of neocarzinostatin inhibited cell growth, with the cell count decreasing from 10^5 /ml at incubation with the antibiotic to $10^{4.8}$ /ml 5 days later. Incubation with neocarzinostatin induced development of giant cells, which began to appear 24 hr after introduction of the compound. Immunofluorescence-positive cells were more frequent in neocarzinostatin-treated cultures than in controls, with the positive cells constituting 28% of cultures 5 days after incubation with 1 μg/ml neocarzinostatin as compared with 11% positive cells in control cultures at that time. This indicated that the percentage of Epstein-Barr virus-bearing cells was higher in neocarzinostatin-treated than in untreated cultures. Counts of virus particles in cultures treated with neocarzinostatin and in control cultures showed that the production of virus particles in treated cultures was higher than in untreated cultures; cell-associated virus particles numbered 8×10^7 /culture at the commencement of neocarzinostatin incubation and 2.8×10^8 after 8 days of incubation. Virus particles in treated and untreated cultures were morphologically similar. The number of cells incorporating ^3H -thymidine was higher in fluorescent (virus-bearing) cells in the presence of neocarzinostatin than in non-fluorescent cells. Apparently, neocarzinostatin inhibits cell division but not viral DNA synthesis or the formation of viral particles in cells; the compound also appears to reduce the synthesis of host cellular DNA.

- 1021 EPSTEIN-BARR VIRAL ANTIGEN IN SINGLE CELL CLONES OF TWO HUMAN LEUKOCYTIC LINES. (E.) Miller, M. H. (Child. Hosp. Med. Ctr., Boston, Mass.), D. Stitt and G. Miller. *J Virol* 6(5):699-701, 1970.

Single cell clones derived from 2 cell lines were assayed for Epstein-Barr virus (EBV) antigen. The cell lines, LS-B and EB₃, were established from the peripheral blood of a child with acute leukemia and from a Burkitt lymphoma tumor. Clones were established from single cells from each of these lines

in the presence of human placental cell feeder layer. All 10 of the clones derived from LS-B cells contained EBV antigen; usually no more than 0.1-0.2% of the cells contained antigen. All EB₃ clones also contained viral antigen, about 1% of cells showing antigen-positive reactions. These findings appear to suggest that the EBV genome is associated with more cells than demonstrate EBV antigen.

- 1022 IMMUNOSUPPRESSION BY LEUKEMIA VIRUSES:
IV. EFFECT OF FRIEND LEUKEMIA VIRUS ON
ANTIBODY-PRECURSORS AS ASSESSED BY CELL TRANSFER
STUDIES. (E.) Ceglowski, W. S. (Temple U. Sch. Med.,
Philadelphia, Pa.) and H. Friedman. *J Immunol*
105(6):1406-1415, 1970.

Immunosuppression induced by leukemogenic Friend virus infected mice spleens were studied for antibody-precursor cells through indirect cell transfer using drug-treated inbred female BALB/c mice as recipients, in an attempt to delineate the mechanism involved. Transfer of cells from normal mice, followed by immunization with RBC, resulted in the appearance of increasing numbers of plaque-forming cells reaching a peak of approximately 5000 at 9 days after cell transfer; drug-treated mice showed similar kinetics of plaque-forming cell appearance but which peaked at a level 50% lower than in control animals. Earliest rise in the appearance of antibody foci occurred on day 3, increasing till day 6 and then declining with consistently fewer foci appearing in spleens of recipient mice given spleen cells from infected donor animals, with the lowest number occurring when the time interval between infection and cell transfer was longest. Although a direct effect of a leukemia virus on antibody-forming cells or their precursors is still speculative, it has been proposed that these viruses may suppress immunity by interfering with specific cellular components of the immune system.

- 1023 STUDIES ON THE INFECTIVITY AND CYTOPATHOLOGY OF EPSTEIN-BARR VIRUS IN HUMAN LYMPHOBLASTOID CELLS. (E.) Durr, F. E. (Dept. Virol. Cancer Res., Pfizer Inc., Maywood, N.J.), J. H. Monroe, R. Schmitter, K. A. Traul and Y. Hirshaut. *Int J Cancer* 6(3):436-449, 1970.

The infective capacity and cytopathic effect of Epstein-Barr virus (EBV) in cultures of human lymphoblastoid cells was investigated. EBV concentrates were prepared from virus-positive Burkitt lymphoma cells (P-3J strain) and from a clone of these cells (HRLK cells). Cell cultures were prepared from normal human peripheral blood, maxillary tumors from Burkitt lymphoma cases, and blood from acute myelogenous leukemia cases. Indicator cells from these cultures were exposed to 0.5-1.0 ml of virus concentrate. All types of culture were successfully infected by the virus, and 2 general types of cytopathic effect were observed. In 1 case, a cytopathic effect was produced which brought about 98% cell death in 4 days. HRLK cells produced the most marked cytopathic effects, usually inducing acute cytopathic effects within 16-72 hr postinfection.

The acute cytopathic effect was characterized by cell swelling, progressive degeneration, and progressive polykaryocyte formation. A less severe cytopathic effect included minimal cell swelling, followed by either the establishment of a carrier culture or of a culture in which virus eventually disappeared. Non-enveloped herpesvirus-type particles were detected in the nuclei of changed cells as early as 16 hr postinfection; virus particles with envelopes could be found in the cytoplasm at a later point. Cells from Burkitt lymphoma and acute myelogenous leukemia showed a less acute cytopathic effect and fewer virus-antigen containing cells than did cells from normal blood. Human sera containing antibodies which reacted with the EBV envelope neutralized infectivity.

- 1024 EPSTEIN-BARR VIRUS IN BURKITT'S LYMPHOMA AND NASOPHARYNGEAL CARCINOMA. (E.) Gunven, P. (Karolinska Inst., Stockholm, Sweden), G. Klein, G. Henle, W. Henle and W. Clifford. *Nature* 228(5276):1053-1056, 1970.

Anti-membrane antigen and anti-Epstein-Barr-viral capsid antigen antibody levels in 96 Burkitt's lymphoma patients in different disease stages were compared with their healthy blood relatives and Africans with chronic tonsillitis. Elevated levels of anti-viral capsid antigen antibody were found in all Burkitt's lymphoma patients compared to 2 groups of healthy relatives and the tonsillitis group; no significant differences were found according to age and sex. A significant elevation of anti-membrane antibody was also noted; a slightly lower mean was seen in patients in remission for 1 yr. The temporary rise of anti-membrane antigen levels after local radiotherapy suggests that continued antigenic stimulation may be important for the maintenance of high anti-membrane antigen antibody levels.

- 1025 EPSTEIN-BARR VIRUS (EBV)-ASSOCIATED ANTIBODY PATTERNS IN MALIGNANT LYMPHOMA AND LEUKEMIA: I. HODGKIN'S DISEASE. (E.) Johansson, B. (Karolinska Hosp., Stockholm, Sweden), G. Klein, W. Henle and G. Henle. *Int J Cancer* 6(3):450-462, 1970.

Epstein-Barr virus (EBV) antibody titers were determined in the blood of patients with Hodgkin's disease. Sera from Swedish patients with Hodgkin's disease and from normal donors were used; EBV was prepared from tumor biopsies from patients with Burkitt lymphoma, and antibody titration in the Hodgkin's disease sera was carried out in indirect immunofluorescence tests. Serum antibodies capable of blocking the direct membrane immunofluorescence reaction between EBV-carrying cell lines and a fluorescein-conjugated serum from a Burkitt lymphoma patient (the F-Mutua conjugate) were tested. Sera from Hodgkin's disease patients had higher titers of EBV antibody and F-Mutua conjugate than normals. In 47% of Hodgkin's disease sera a high EBV antibody titer (greater than 160) was found, compared to 17% of normal sera with high titers. Patients over 40-yr-old of both sexes had higher

ers of EBV antibody than did younger patients. titers of EBV antibody were found in Hodgkin's disease patients with paraganuloma (15% of patients having titers in excess of 160), granuloma, and sarcoma (83% of Hodgkin's sarcoma patients having titers in excess of 160). These findings showed an inverse relationship between abundance of lymphoid cells and EBV-associated serological reactivity. A similar relationship was found for patients having varying degrees of clinical symptomatology associated with Hodgkin's disease, including constitutional symptoms, low or high peripheral lymphocyte counts and slow or rapid sedimentation rates.

POLYRIBOSOMES AND MESSENGER RNA OF AVIAN VIRUS-INDUCED LEUKEMIA CELLS. (Fr.)
 Ger, C. (Gustave Roussy Inst., Villejuif, France), J. Imbenotte, F. Lacour and J. Harel. *Ann Inst Pasteur* 119(3):384-396, 1970.

Sedimentation characteristics of polyribosomes isolated from AMV-infected brown leghorn chicken leukemic cells (virus-producing myeloblasts from peripheral blood) were compared to those from bone marrow myeloblasts of normal 5-day-old baby chickens. Amount of polyribosomes with a sedimentation coefficient above 250 S was much higher in leukemic cells than in normal cells. The pulse-labeled RNA (32 P) in normal cell polyribosomes exhibited a peak of radioactivity in the 5-10 S fraction (centrifugation in 0.14 M NaCl or 0.05 M NaCl), while RNA from leukemic cell polyribosomes showed a peak in the 18 S fraction. The labeled polyribosomal RNA from leukemic cells of the fraction with a sedimentation coefficient above 18 S constituted 58-62% of the total radioactivity of RNA; this fraction ranged between 12 and 32% in normal cells. The nucleotide composition of the RNA from all centrifugal fractions from both normal and leukemic cells revealed similar levels of uridine nucleotide (approximately 30%), and lower amounts of adenine nucleotide (approximately 20 mole %). The 18-26 S fraction of polyribosomes from leukemic cells exhibited a lower content of guanosine and cytidine than the corresponding fraction from normal cells. The relationship between the higher amounts of heavy messenger RNA found in polyribosomes from leukemic cells to malignancy is not certain.

THE N-TERMINAL AMINO ACID SEQUENCE OF TWO AVIAN LEUKOSIS GROUP SPECIFIC ANTIGENS.
 Niall, H. D. (Massachusetts Gen. Hosp., Boston), G. Bauer and D. W. Allen. *Proc Nat Acad Sci* 67(4):1181-1186, 1970.

Two major group-specific antigenic proteins from avian leukosis virus have been compared by amino acid analysis, tryptic peptide fingerprinting and N-terminal sequence determination. Amino acid composition of group-specific antigen showed high values of alanine, leucine and glutamic acid for gs-a, whereas gs-b showed high values of leucine, glycine and aspartic acid, resp., indicating that these are distinct proteins with unique amino acid sequences; there was some similarity between residues 14-20 of gs-a

and residues 11-19 of gs-b. Sequence microheterogeneity was detected at residue 6 of gs-b, with both threonine and glutamic acid present in approximately equivalent amounts. This glutamic acid-threonine substitution is present in both tobacco mosaic virus and bacteriophage coat proteins.

1028 ANTIGEN COMMON TO A HERPES TYPE VIRUS FROM CHICKENS WITH MAREK'S DISEASE AND EB VIRUS FROM BURKITT'S LYMPHOMA CELLS. (E.) Ono, K. (Res. Inst. Microbial Dis., Osaka U., Japan), S. Tanabe, M. Naito, T. Doi and S. Kato. *Biken J* 13(3):213-217, 1970.

Double-diffusion precipitation tests demonstrated that herpes type virus isolated from a chicken with Marek's disease and Epstein-Barr virus (EBV) isolated from Burkitt's lymphoma cells shared a common antigen. Antisera for use in the immunodiffusion tests were prepared from adult humans with EBV-positive sera. Similar antigen lines were formed between EBV-positive human sera and the EBV antigen, and between EBV-positive human sera and chick herpes virus antigen. No antigen line was formed by either chicken herpes virus or EBV with any sera from chickens raised in vinyl isolators or with sera against duck embryo fibroblasts.

1029 PROPAGATION OF HERPES TYPE VIRUS ISOLATED FROM CHICKENS WITH MAREK'S DISEASE IN JAPANESE QUAIL EMBRYO FIBROBLASTS. (E.) Onoda, T. (Res. Found. Microbial Dis. Osaka U., Japan), K. Ono, T. Konobe, M. Naito, Y. Mori and S. Kato. *Biken J* 13(3):219-228, 1970.

The virological properties of a herpes-type virus grown in Japanese quail embryo fibroblasts (QUEF) were investigated; the virus had been isolated in duck embryo fibroblasts from a chicken with Marek's disease. In QUEF cultures, the characteristic morphological changes brought about by the virus were foci consisting of round refractile cells and multinucleate giant cells. When herpes-type virus-infected QUEF cultures were inoculated with anti-quail red blood cell serum and quail red cells, mixed agglutination was observed and almost all cultured cells were affected. No mixed agglutination was observed when infected QUEF cultures were tested with anti-quail red cell serum and duck red cells, indicating that the herpes-type virus-infected QUEF culture consisted exclusively of quail cells at the passage level examined. No infectious virus could be found in the supernatants of infected cultures, and no virus could be extracted by sonic or temperature-disruption of cells, indicating that the virus in infective QUEF cells was not cell-free. The propagation of virus in cell cultures was inhibited by 5-iododeoxyuridine. DNA synthesis occurred only in the nuclei of infected cells, as revealed by autoradiography with 3 H-thymidine. Hematoxylin-eosin staining revealed herpes-type intranuclear inclusion bodies in infected cells, and herpes virus antigen was demonstrated by the direct fluorescent antibody method in both cytoplasm and nucleus. Although the virus produced

plaques on monolayers of either QUEF or duck embryo fibroblast cells, the number of plaques in the QUEF monolayer was approximately $2 \log_2$ less than the number of plaques in the duck monolayer. Infected QUEF was injected into the chorioallantoic membrane of embryonated hen's eggs, with the result that the inoculated cells produced pocks on the membranes within 7-8 days after inoculation.

- 1030 ISOLATION OF HERPES TYPE VIRUS FROM CHICKENS WITH MAREK'S DISEASE USING DUCK EMBRYO FIBROBLAST CULTURES. (E.) Kato, S. (Res. Inst. Microbial Dis., Osaka U., Japan), K. Ono, M. Naito, T. Doi, N. Iwa, Y. Mori and T. Onoda. *Biken J* 13(3):193-203, 1970.

The characteristics of a Herpes type virus isolated from chickens with Marek's disease were investigated. Chicken blood from birds with Marek's disease was cultured with duck embryo fibroblasts, and viral cytopathic agents were isolated from cultures. Cytopathic agents produced foci characterized by refractile rounded or shrunken spindle cells and syncytial type giant cells. In the infected duck embryo fibroblast cultures, these foci exhibited typical herpes type intranuclear inclusions and intracytoplasmic eosinophilic inclusions, as revealed by hematoxylin-eosin staining. Labeling studies with ^3H -thymidine showed that DNA synthesis continued in the nuclei of the cells in the infectious foci; cells in these foci showed specific fluorescence using the fluorescent antibody technique. Supernatants from infected cultures apparently contained no infectious agent, and ultrasonic disintegration abolished the infectivity of a virulent infected duck embryo fibroblast suspension. Electron microscopy revealed naked particles similar to those of herpes virus in infected foci, as well as occasional particles with an additional membrane. Morphologically, particles consisted of a hexagonal capsid and a central core, reminiscent of herpes virus particles. Inocula containing intact cells was required in order to induce the cytopathic effect by viral agents in cell cultures. The cytopathic agents could not be shown to have transforming activity. Although herpes type virus was recovered after inoculation into day-old chicks, duck embryo fibroblast-passaged herpes type virus apparently had no pathogenic efficacy for chickens.

- 1031 DEMONSTRATION OF A HERPES-TYPE VIRUS IN SHORT-TERM CULTURED BLOOD LYMPHOCYTES ASSOCIATED WITH MAREK'S DISEASE. (E.) Campbell, J. G. (Brit. Empire Cancer Campaign Res., Edinburgh, Scotland) and G. N. Woode. *J Med Microbiol* 3(3):463-473, 1970.

Lymphocytes were cultured from chickens with Marek's disease and examined by electron microscopy. Cultures exhibited a blast form in 72-96 hr, with transformation of about 4% of the cultured lymphocytes into blast cells. Transformed cells, which came from chickens with classical Marek's disease, were 2-4 times the size of unaltered lymphocytes and showed large, often misshapen, vesicular nuclei,

marginated chromatin, and occasional disruption of the nuclear membrane. Typical, hexagonal, herpes-type virus particles were present in many of the transformed cells. Most of the particles were immature and had a single envelope surrounding a nucleoid of variable density. Empty and double-enveloped particles were also seen, but the latter rarely. Some virus particles were associated with intranuclear filaments, which may have been the product of aberrant viral replication. Some untransformed cells also showed granule-lamellar arrays in the cytoplasm, possibly representing the inner structure of the filaments. When kidney cells from healthy chicks were incubated with lymphocytes cultured from birds with Marek's disease, a cytopathic effect was produced within 3 wk. The reaction was necrotic, with microplaques and long delicate cytoplasmic threads extending across the plaque. Similar results were obtained using fresh lymphocytes or tumor cells from cases of acute Marek's disease. Indirect immunofluorescence showed that a high proportion of transformed lymphocytes from cases of Marek's disease contained a viral antigen, as did the kidney cells in the region of the cytopathic effect. Transformed lymphocytes from cases of acute Marek's disease with gonadal tumors also included a herpes-type virus.

- 1032 PROTEIN SYNTHESIS IN NORMAL, X-IRRADIATED AND FRIEND VIRUS INFECTED MOUSE SPLEEN NUCLEI. (E.) Munson, B. R. (Roswell Park Mem. Inst. Springville, New York) and R. J. Fiel. *Res Commun Chem Path Pharmacol* 1(4):517-525, 1970.

The incorporation of amino acids in the nuclei of normal, X-irradiated, and virus-infected cells was investigated. Mice were exposed to whole-body irradiation (60 rads/min) or injected with 0.2 ml of a 10% spleen homogenate infected with Friend virus. At various times thereafter, mice were killed and amino acid incorporation in the nuclei of their spleen cells was assayed. When *in vitro* incorporation of amino acid into nuclei isolated from normal and Friend virus-infected mice were compared, it was seen that nuclei isolated from infected mice incorporated less amino acids than normal cells. Amino acid incorporation in nuclei from mice infected 4 days earlier was similar to that from normal mice. However, the rate of amino acid incorporation in nuclei from cells infected 25 days earlier was less than 50% that of normal cells. In nuclei isolated 4 days after X-irradiation amino acid incorporation was stimulated 6-fold over that of normal controls, while in nuclei isolated 18 days after X-irradiation the rate was stimulated 3-fold.

- 1033 ERYTHROCYTE OSMOTIC FRAGILITY IN FRIEND VIRUS-INFECTED MICE. (E.) Parr, I. B. (Chester Beatty Res. Inst., Sutton, Surrey, England) and K. E. K. Rowson. *Europ J Cancer* 6(5):411-415, 1970.

Osmotic fragility was investigated in the erythrocytes of mice infected with Friend leukemia virus (FLV). Erythrocyte osmotic fragility was deter-

ed by exposing erythrocytes from virus-infected mice to various concentrations of buffered saline pH 7.4; the ability of the spleens of normal and virus-infected mice to take up ^{14}C chromium-labeled erythrocytes was also studied. When normal and infected erythrocytes were incubated in saline for 30 min, infection with FLV could not be shown to affect erythrocyte fragility until late in the course of the disease, at which point there was still no change in the mean concentration of saline causing 50% erythrocyte lysis. However, in cells incubated for 30 min, there was an increase in the proportion of erythrocytes which were both more and less fragile than the average. When normal and virus-infected erythrocytes were incubated for 72 hr, erythrocytes from infected mice appeared to lyse more readily than normal erythrocytes; there was an increase in mean osmotic fragility of erythrocytes as early as 15 days after virus injection. Tonicity causing 50% lysis in normal and infected erythrocytes incubated in saline for 72 hr was 0.65 and 0.68 on day 15 after virus injection, and 0.74 on day 23 after virus injection. Splenectomized mice, survival after FLV injection was prolonged, and the onset of increased osmotic fragility and anemia were delayed but not prevented. Erythrocytes labeled with ^{14}C chromium were taken up by the spleen of FLV-infected mice about twice as rapidly as they were taken up by the spleen of normal mice (6.3% and 3.5%, resp.).

4 WILD-TYPE GROSS LEUKEMIA VIRUS AND THE PATHOGENESIS OF THE GLOMERULONEPHRITIS OF ZEALAND MICE. (E.) Mellors, R. C. (Hosp. Spec. Lab., New York, N.Y.), T. Shirai, T. Aoki, R. J. G. and K. Krawczynski. *J Exp Med* 133(1):113-119, 1971.

A hypothesis that spontaneous glomerulonephritis in NZB and (NZB x NZW) F_1 hybrid mice is associated with the formation by the mice of natural antibodies against antigens of Gross leukemia virus was tested. Kidney homogenates and kidney eluates from mice of these strains were assayed for the presence of Gross virus antigens and antibodies. Only mice having glomerulonephritis demonstrated by proteinuria were used. Soluble antigen was detected in the plasma and eluate of mice with proteinuria from 8-14 months of age. G natural antibody was found in none of the kidney homogenates, but in all of the kidney eluates. Tests for antinuclear antibody, anti-erythrocyte antibody and G natural antibody were performed on acid-eluate of kidneys of NZB mice, with the result that the normalized titer of G natural antibody in the kidney eluate was 25 and 12 in the serum. Titer of antinuclear antibody in kidney eluate was 25 and 32 in the serum. Anti-erythrocyte antibody titer in kidney eluate was 25 and 56 in the serum. (NZB x NZW) F_1 hybrid mice were positive for complement-fixing murine leukemia virus antigens. Hybrid mice developed glomerulonephritis and produced soluble antigens and free G natural antibodies earlier in life than did NZB mice. As G soluble antigen was progressively eliminated from hybrid mice, the proteinuria manifestation of glomerulonephritis became increasingly conspicuous. Gross

leukemia virus-specific antigens and bound immunoglobulins were found in glomerular lesions of hybrid mice, both in the mesangium and in the wall of the peripheral capillary loop of the glomeruli. Apparently, the pathogenesis of glomerulonephritis is related to the formation of antibodies against Gross virus antigens, and specifically to the deposition of immune complexes of G natural antibodies with G soluble antigen in the glomeruli.

1035 INCREASED INCIDENCE OF LYMPHOMA IN C3H/HeJ ADULT MICE INJECTED WITH GROSS VIRUS AND ANTITHYMOCYTIC SERUM. (E.) Vredevoe, D. L. (Sch. Nurs., U. California, Los Angeles) and E. F. Hays. *Infect Immun* 2(6):723-726, 1970.

The effect of antithymocyte serum (ATS) on the development of lymphomas in mice injected with Gross leukemia virus was investigated. Mice were given regimens of 1-4 weekly i.p. doses of cell-free filtrate of a Gross virus-induced lymphoma and 0.2 ml doses of ATS; controls were given cell-free filtrate and normal rat serum in place of ATS. The incidence of lymphoma was higher in each of the ATS-treated groups than in controls. Incidence of lymphoma increased as the number of cell-free filtrate doses increased; the maximum incidence was attained at 3 injections of cell-free filtrate, at which point 79% of rats in the ATS group showed lymphomas, compared to less than 50% of rats given normal rat serum. Rats given 3 and 4 doses of ATS had markedly shorter latent periods for the development of lymphomas than rats given normal rat serum; at 4 doses, latency for ATS-treated rats was 119-266 days, and latency for controls was 239-298 days.

1036 AN IMMUNOFLUORESCENT FOCUS ASSAY FOR GROSS LEUKEMIA VIRUS. (E.) Woods, W. A. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), J. Massicot and M. A. Chirigos. *Proc Soc Exp Biol Med* 135(3):772-777, 1970.

An immunofluorescent focus assay technique for Gross leukemia virus was developed which demonstrated Gross leukemia virus in tissues and fluids of AKR strain mice, and which permitted the assay of virus-neutralizing antibody in tissue cultures. Viruses in cell suspensions were frozen and thawed, and sera were diluted in 10% fetal calf serum and inactivated at 56° before testing. Equal volumes of serum and virus were mixed and incubated, and 0.1 ml of virus-serum mixture was inoculated onto three-ring cultures on slides; slides were then incubated. Anti-Gross leukemia virus serum was prepared in rats, and immunofluorescent staining was carried out according to standard procedures. Diffuse foci of strongly fluorescent cells were observed in cultures infected with Gross virus after staining with rat-anti-Gross leukemia virus serum or rat anti-murine sarcoma virus serum. Blocking experiments showed that staining of cultures infected with viruses other than Gross virus with anti-Gross virus serum produced fluorescent staining of almost all cells, and that staining was due to the group-spe-

cific antigen. Inoculation of Gross virus onto cultures of mouse cells from various sources produced titrations of between 2×10^1 and 4×10^5 focus forming U/ml culture 7-35 days after inoculation.

- 1037 RNA-DEPENDENT DNA POLYMERASE ACTIVITY IN FIVE RNA VIRUSES: DIVALENT CATION REQUIREMENTS. (E.) Scolnick, E. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), E. Rands, S. A. Aaronson and G. J. Todaro. *Proc Nat Acad Sci* 67(4): 1789-1796, 1970.

This study compares the effects of manganese and magnesium on DNA synthesis by RNA-dependent DNA polymerase in Rauscher leukemia virus. Synthesis of DNA from viral RNA of intact virions occurred equally well with either magnesium acetate or manganese acetate. However, at limiting concentrations of divalent cation (1×10^{-3} M) manganese was more effective; with synthetic RNA polymer used as template, a 50- to 100-fold stimulation of activity occurred in the presence of manganese with optimal concentrations for synthesis from endogenous viral RNA being too high for optimal synthesis with the synthetic template. At either 4×10^{-3} M magnesium or 4×10^{-3} M manganese, DNA synthesis from endogenous viral RNA is optimal. Conditions that are optimal for detecting polymer-stimulated activity in murine leukemia virion are effective for murine mammary tumor virus and avian myeloblastosis virion. Two nononcogenic viruses, visna virus and primate syncytium-forming virus, exhibit similar DNA polymerase activity.

- 1038 RAUSCHER VIRUS AND ITS EFFECT ON RNA SYNTHESIS IN SPLEEN CELLS OF BALB/c MICE. (Rus.) Kiselev, F. L. (Acad. Med. Sci. USSR, Moscow), G. G. Shatalova, L. A. Semenova, N. A. Varich and I. S. Irlin. *Vop Virus* 15(5):589-596, 1970.

The presence of a specific RNA_x fraction in mouse spleen cells during the early stages of Rauscher virus-induced leukemogenesis was ascertained. Experimental BALB/c mice were inoculated i.v. with Rauscher virus at a 1:1000 dilution which led to the development of more than 50 colonies in the spleen. Spleen cells were isolated at various stages of leukemogenesis and RNA was extracted after double phenolic deproteinization. No differences in sucrose gradient sedimentation characteristics were noticed between RNA preparation from normal and infected cells. Further fractionation on cellulose columns for the segregation of double- and single-stranded RNA showed within the single-stranded fraction the presence of an additional fraction called RNA_x, with a buoyant density of 1.6 in a cesium sulfate gradient. This density was lower than that of the usual single-stranded RNA and was typical for the intermediate replicative forms in animal viruses; it was also indicative of a more ordered configuration with respect to the usual single-stranded RNA. Sucrose gradient centrifugation situated RNA_x at the level of the 28 S

ribosomal RNA with a shoulder having a lower sedimentation constant, indicating its heterogeneity and precluding the determination of its molecular weight from the sedimentation characteristics. RNA_x was found in both normal and infected spleen cells; substantially higher amounts were found in the latter. Studies of the effect of viral infection on the accumulation of RNA_x in various stages of leukemogenesis showed RNA_x reaching a peak (12-14% of the total single-stranded RNA) on the 3rd day following inoculation and decreasing thereafter. Levels of RNA_x accumulation were dependent on the amount of Rauscher virus inoculation. This phenomenon was noticed only in Rauscher virus replication susceptible systems such as BALB/c mouse spleens and did not occur in C57BL/6 mouse spleens which are resistant to Rauscher virus infection.

- 1039 ELECTRON MICROSCOPIC STUDY OF THE GUINEA PIG LEUKEMIA VIRUS. (E.) Feldman, D. G. (VA Hosp., Bronx, N.Y.) and L. Gross. *Cancer Res* 30(11):2702-2711, 1970.

The structure of virus particles and their distribution, formation and location in relation to cell components in the guinea pig are described and compared to particles found in mouse leukemia. Strain 2 and F₁ hybrid guinea pigs were inoculated subcutaneously with 10 or 20% leukemic cell suspension and leukemic plasma. All inoculated animals developed stem cell leukemia and were sacrificed when the disease was fully developed 14 to 46 days after inoculation at which time peripheral blood counts exceeded 250,000 to 3,000 WBC/mm³. Fragments of various organs of leukemic animals and non-inoculated control animals were removed and processed for electron microscopic studies and for routine light microscopy. All leukemic animals revealed leukemic virus particles in the tissue examined. Immature virus particles with electron-lucent centers and two concentric shells were observed budding from the membranes or free within the cisternae of the endoplasmic reticulum. Mature virus particles with electron-dense nucleoids and single, thick outer shells were found mainly in the intercellular spaces. Structurally these differed from mouse leukemia virus which presents a relatively thin and smooth unit membrane of the outer coat and a nucleoid which varies from opaque to electron-lucent and often exhibits pleomorphism. A process of reverse pinocytosis may possibly describe the movement of particles from the interior to the periphery of the cell.

- 1040 VIRUS-INDUCED MYELOGENOUS LEUKAEMIAS OF THE MOUSE: ELECTRON MICROSCOPIC AND MORPHOMETRIC STUDIES. (Ger.) Fritsch, R. S. (German Acad. Sci., Berlin, Germany). *Veroeff Morph Path* 48:1-128, 1971.

Electron microscopy and morphometry applied to the study of the morphology and leukemogenesis of Graffius virus-induced myelogenous leukemias in AB/Jena mice revealed the number of cytoplasmic myeloid granules per area unit (Zgr) as the most appropriate ultra-

structural parameter for the characterization of the stages of myelogenous cell maturation. Myelogenous leukemias were thus classified into undifferentiated (myeloblastic and paramyeloblastic leukemias), moderately differentiated (of which 90% are chloroleukemias), well-differentiated myelogenous leukemias (in which 76% of cell infiltrates appear yellowish); the defining characteristics in the 2 latter cases were associated with their verdoperoxidase contents. All leukemias presented intercellular C-type virus particles and intramegakaryocytic A₃-type virus particles. Crystalline inclusions (20-25 Å diameter) were observed within phagocytes and kidney tubular cells in some of the well-differentiated leukemias; these inclusions were considered to be protein containing deposition products of hemoglobin resulting from erythrocytic degeneration. The first passage of cell-mouse reticuloendothelial ascites sarcoma filter (RAB-1), inoculated into 136 mice, induced exclusively myelogenous leukemia in 50% of the animals. Serial filtrate passages (5 or 6) led to an increase in virulence and induced diversification into several genetic types of induced leukocytoses in 89-95% of infected animals. Morphometrical ultrastructural analysis allowed detection of quantitative differences between normal granulocytopenia and the corresponding preleukemic process; an ultrastructural morphological myelogram was established using the frequency distribution of the relative number of cytoplasmic vacuoles (Zgr).

THE EFFECT OF ACID DEOXYRIBONUCLEASE ON THE LEUKOCYTES AND BONE MARROW CELLS OF PS-MICE INDUCED LYMPHOBLASTIC LEUKEMIA IN PS-MICE.

(Rus.) Eschenbach, C. (Child. Clin. U. Marburg, Germany), G. Ludwig, W. Kühnel and C. Förster. *Immunologie* 2(3):387-402, 1970.

The effect of deoxyribonuclease (DNase II) on the leukocytes of peripheral blood and on bone marrow cells of PS mice with virus-induced lymphoblastic leukemia is described. The mice were inoculated at the age of 3 wk with an organ extract of leukemic infiltrated lymph nodes and spleen containing lymphoblastic leukemia cells from a leukemic mouse of the same strain. A large percentage of the inoculated mice revealed lymphoblastic leukemic cells in their peripheral blood 3 or 4 wk after the inoculation with a count of 50,000/mm³ within a few days. The DNase II activity of 100 Kunitz units was injected at various intervals. The results showed that the DNase II had a cytotoxic effect on the lymphoblastic leukemia cells, and these cells were affected more severely than the neutrophilic granulocytes and lymphocytes of the healthy mice. In the healthy mice, as well as in the animals in the preleukemic stage of the disease, the DNase II (16 x 0.4 mg/kg), induced a decrease in the leukocyte count 48 hr after administration in the peripheral blood of 60% of the initial value; the leukemic mice reacted with a decrease of 90 to 95%. The marked cytotoxic effect of the enzyme on the leukemic cells is evident from the temporary shrinkage of the infiltrate quantity at the site of inoculation where necrosis of single cells is seen; during this period an increase in granulopoiesis and myelopoiesis was observed in the

bone marrow. Deoxyribonuclease appears to have a greater cytotoxic effect on lymphoblastic leukemia cells than on normal leukocytes.

- 1042 IMMUNOSUPPRESSIVE EFFECTS OF DNA VIRUSES: PAPOVA VIRUS AND HUMAN ADENOVIRUS TYPE 16. (Rus.) Gamburg, V. P. (Acad. Med. Sci., USSR, Moscow), O. E. Shcherbakova and G. Ya. Svet-Moldasky. *Vop Virus* 15(5):612-614, 1970.

Immunosuppression response to inoculation of live Sendai virus into animals previously inoculated with SV40 and adeno type 16 viruses was studied in Syrian male hamsters 2 months of age. Antibodies to Sendai virus were determined at various intervals following immunization. The average antihemagglutinin titers expressed logarithmically were much lower in the SV40 or adeno type 16 virus inoculated hamsters than in the control animals which were immunized with Sendai virus only 15 and 23 days following specific immunization. Another experiment was performed with hamsters treated as follows: 1) immunized with Sendai virus following inoculation with SV40 virus, 9 days earlier; 2) immunized with Sendai virus following previous inoculation with uncontaminated green monkey kidney culture media; 3) immunized with Sendai virus only; 4) simultaneously immunized i.p. with SV40 and Sendai virus. The levels of specific antihemagglutinins in sera of group 1 hamsters were much lower than in those inoculated with Sendai virus only (group 3). Simultaneous inoculation with SV40 and Sendai virus (group 4) or inoculation with culture media of green monkey kidney (group 2) had no effect on the specific antibody levels of the sera. The immunosuppressive effect manifested by these viruses appears to support a carcinogenic mechanism in which immunosuppression constitutes one of the conditions for the occurrence of malignancy.

- 1043 STRUCTURAL PROTEINS OF ADENOVIRUSES. (E.) Petterson, U. (Wallenberg Lab., U. Uppsala, Sweden). *Acta Univ Uppsala* 89:1-21, 1970.

Adenovirus capsid proteins were obtained in purified form and characterized. Adenovirus hexon antigens were purified from infected KB cells and characterized by analytical ultracentrifugation, immunodiffusion, and electron microscopy. The hexons had the form of prolate ellipsoids, probably with cylindrical shapes measuring 76 x 119 Å, and a molecular wt of 400,000. The hexons were found to be free of carbohydrates, contained 0.5-0.8% half-cystine, and had a general amino acid composition similar to that of the whole virion, except that the virion had a higher arginine content than the hexon; no free N-groups were found on the hexon polypeptide chain. Antisera prepared with the purified hexon did not contain significant amounts of neutralizing antibodies, in contrast to antisera prepared with hexons which were partially purified. Fiber antigen from adenovirus was purified as was hexon antigen. The form of the fiber antigen was that of an extended structure with a knob at the end, and the molecular wt of the single type of

polypeptide detected was 70,000. High titers of neutralizing antibodies were observed for antisera against purified fiber antigens when neutralization was measured with focus-forming unit assay, while the plaque assay gave only insignificant titers. Purified penton antigens appeared as complex units each with a 90 Å base and a 200 Å projection, and some units had pentagonal outlines; the molecular wt of the penton was 400,000. The bonds between fiber and penton base were not covalent; fibers could be dissociated from bases by an 8% pyridine soln. Intact pentons and their free bases caused a cytopathic effect when added to monolayer cultures of KB cells.

- 1044 CELLULAR DNA SYNTHESIS IN PRODUCTIVE INFECTION WITH ADENOVIRUSES. (E.) Takahashi, M. (Res. Inst. Microbial Dis., Osaka U., Japan), K. Baba and Y. Minekawa. *Int J Cancer* 6(3):399-409, 1970.

The effect of adenoviruses on cellular DNA synthesis (^3H -thymidine incorporation and DNA-DNA hybridization studies) in productive infection of hamster kidney cells (HamK) and human embryonic lung cells (HEL) was investigated. After 24 hr adenovirus type 5 (Ad5)-infected HamK cells that had been treated with 5-fluorouracil (FU, 13 $\mu\text{g}/\text{ml}$) and thymidine (0.5 $\mu\text{g}/\text{ml}$) showed lower ^3H -thymidine incorporation than untreated cells (2.8 and 9 cpm/ μg DNA $\times 10^4$, resp.), but remained higher than uninfected cells treated with FU or untreated (1.3 and 0 cpm/ μg DNA $\times 10^4$, resp.). The newly synthesized ^3H -DNA was mainly cellular DNA between 16 and 32 hr after infection in FU-treated cultures, and synthesis of viral DNA was delayed and reduced in FU-treated cells (560 cpm after 28-32 hr compared to 3,343 cpm in untreated cells). When long-term labeling of DNA was studied in the presence of hypoxanthine, aminopterin, and glycine (to prevent endogenous biosynthesis of thymidylic acid), incorporation of counts into cellular DNA was 3 times higher in Ad5-infected cells (12,488 cpm) than in uninfected cells (4,337 cpm) suggesting that cellular DNA synthesis was stimulated by infection. Incorporation of ^3H -thymidine into cellular DNA in monolayer cultures of HEL infected with adenovirus types 2, 3, 4, 5, and 12 was 2-6 times higher than uninfected cultures 16-40 hr after infection, and the stimulation was detectable for prolonged periods (88-112 hr after infection), suggesting that the induction of cellular DNA synthesis by the infection had occurred.

- 1045 PRODUCTION OF HIGH TITRES OF INTERFERON IN CHICKEN LEUKOCYTES INOCULATED WITH HUMAN ADENOVIRUS TYPE 12. (E.) Mucsi, I. (U. Med. Sch. Szeged, Hungary), R. Pusztail, I. Beladi and M. Bakay. *Acta Virol* 14(6):453-458, 1970.

The effect of infection with human adenovirus type 12 on interferon production in chicken leukocytes was investigated. Chicken leukocyte cultures were prepared and inoculated with $2 \times 10^{4.5}$ TCD₅₀ of adenovirus type 12. Adenovirus induced maximal

interferon titers when the concentrations of leukocytes were high; at concentrations of $12-14 \times 10^6$ cells/ml culture fluid, interferon titers were 5-8 (\log_2 values.) At lower concentrations of cells, interferon production was proportionally lower (interferon titers of 1 and 2 (\log_2) at concentrations of 8 and 10×10^6 leukocytes, resp.). Chicken leukocytes retained their interferon-producing ability after incubation at 36° for 48 hr (titers of 1024). When leukocytes were cultured with calf serum and then inoculated with virus, it was found that a serum content of 2.5% or more was required to produce higher titers of interferon (titer of 512 at 2.5% serum concentration); titers of interferon increased when serum concentrations were increased to 20% (interferon titer of 2049 at 20% concentration). Treatment of leukocytes with chloroquine (30 $\mu\text{g}/\text{ml}$) reduced interferon, and treatment with 40 μg chloroquine completely inhibited interferon production in cells inoculated with adenovirus. When viruses were treated with trypsin and then inoculated in leukocyte cultures, interferon production continued, but at reduced levels of efficiency. Leukocytes infected with human adenovirus type 12 apparently release a synthesized and not a preformed interferon.

- 1046 INHIBITION OF ADENOVIRUS REPLICATION BY CANAVANINE. (E.) Neurath, A. R. (Wyeth Lab., Philadelphia, Pa.), F. P. Wiener, B. A. Rubin and R. W. Hartzell. *Biochem Biophys Res Commun* 41(6):1509-1517, 1970.

The effect of canavanine on adenovirus replication *in vitro* was investigated. Adenovirus was cultured in human embryonic kidney cells to which arginine had been added in concentrations of 0.01 mM. Canavanine labeled with ^{14}C was added to cultures in amounts of 1 $\mu\text{mole}/\text{ml}$ culture, and the incorporation of ^3H -thymidine into DNA, the synthesis of viral capsid components and virions, and the synthesis of virus-specific tumor antigens were determined. Addition of canavanine decreased but did not prevent the incorporation of ^3H -thymidine into DNA of adenovirus-infected cells. Rate zonal centrifugation showed that the proportion of label incorporated into viral DNA was 6 and 13% of control when canavanine was added 14 and 24 hr, resp., after virus infection of culture. Apparently, canavanine prevented the initiation of viral DNA synthesis but did not prevent the transient increase of cellular DNA synthesis in infected cells. Canavanine also inhibited the formation of viral capsid components, including pentons, dodecons, and hexons. However, addition of canavanine to cells at the time of infection or later did not prevent the synthesis of adenovirus tumor antigens. Inhibition of adenovirus replication by canavanine was reversible; when canavanine was added at the time of virus infection and withdrawn 2-24 hr later, virus was synthesized but the eclipse period was prolonged by the amount of time canavanine was present. Canavanine added to cultures after the onset of DNA replication partially inhibited DNA synthesis and synthesis of capsid components, and completely blocked the assembly of both into virions.

7 THE RESPONSE OF BHK21 CELLS TO INFECTION WITH TYPE 12 ADENOVIRUS: IV. ACTIVATION DNA-SYNTHESIZING APPARATUS. (E.) Zimmerman, J. Jr. (Rutgers Med. Sch., New Brunswick, N.J.), Raska, Jr. and W. A. Strohl. *Virology* 42(4): 7-1150, 1970.

effect of infection with adenovirus type 12 on synthesis and on various enzyme systems was investigated in hamster cells. Hamster cells were infected with adenovirus type 12 to the point at 89% of cells stained positive for tumor antigen in immunofluorescent staining tests. DNA synthesis began to increase sharply at 12 hr after infection, rising from 1.80 cpm ^3H -thymidine incorporated $\times 10^{-3}/10^6$ cells at 12 hr to 13 cpm $\times 10^{-3}/$ cells at 21 hr; thereafter, DNA synthesis declined quickly, approaching the values for DNA synthesis in uninfected cells at 51 hr postinfection. Thymidine kinase activity reached its maximum level at 16 hr postinfection (10 nmoles of midylate/mg protein/10min). Increases of 136% and 72% were recorded for deoxycytidylate deaminase activity and for cytidine-5'-diphosphate reductase activity, resp., in virus-infected cells. DNA polymerase activity was increased in infected cells compared with controls; at 45 min postinfection, ^3H -TPP incorporation for infected and control cells, resp., were 2900 and 1500 cpm/mg protein.

8 GLYCOLYSIS IN ADENOVIRUS-INFECTED RAT CELL CULTURES AND IN ADENOVIRUS TYPE 12-INDUCED HAMSTER SARCOMA CELLS. (Rus.) Ageyenko, A. I. (P. A. Herzen Sci. Res. Inst. Oncol., Moscow, USSR), N. M. Imukhamedova, V. T. Timofeyev, I. Ya. Kogan and N. Saprin. *Vop Onkol* 16(9):49-53, 1970.

Glycolysis was studied in rat embryo fibroblast (REF) monolayer cultures following inoculation with human adenovirus type 12, with the weakly oncogenic adenovirus type 3 and with the nononcogenic infectious adenovirus type 6; similar studies were done with *in vitro* cultivated adenovirus type-12 induced hamster sarcoma cells. Glucose utilization and lactic acid formation were the parameters followed. Control cultures were obtained with noninfected REF cultures, REF cultures inoculated with inactivated (56°C for 30 min) viruses or with virus-free inoculum medium. Intensified glycolysis was noticed in all cell cultures 2-4 hr following inoculation; it appeared most intense in adenovirus type 12-inoculated REF cultures. Glucose which was utilized in both inoculated and control cultures was completely converted into lactic acid under anaerobic conditions. Aerobic glycolysis occurring in both normal and virus-inoculated cultures was 3 times higher in adenovirus type 12-infected REF cultures and in adenovirus type 12-induced hamster sarcoma cell cultures compared to control cultures. Nearly complete conversion of glucose to lactic acid occurred under aerobic conditions in the case of the adenovirus type 12-inoculated cells while other glucose oxidation pathways seemed to be followed partially in the adenovirus types 3-6-inoculated REF cultures. The ratios between lactate and glucose under aerobic conditions 72 hr following inoculation were 0.7 in the control, 1.96

in the adenovirus type 12, 1.1 in the adenovirus type 3, 1.0 in the adenovirus type 6-inoculated REF cultures and 1.48 in the adenovirus type 12-induced hamster sarcoma cell cultures. The glycolytic shifts in both adenovirus type 12-inoculated REF culture and in the sarcoma cell cultures seemed to be similar. The amount of monolayer cells decreased slowly in the adenovirus type 6-infected culture while no such variations occurred in the adenovirus type 3 and 12 inoculated REF cultures.

1049 PROPERTIES OF THE TRANSFER RIBONUCLEIC ACID METHYLASE ACTIVITY *IN VITRO* OF HAMSTER TUMORS INDUCED BY ADENOVIRUS-12: BASE ANALYSIS. (E.) McFarlane, E. S. (Dept. Microbiol., Dalhousie U., Halifax, Nova Scotia, Canada) and C. G. Lee. *Biochem J* 120(3):499-503, 1970.

The *in vitro* tRNA methylase activity (the bases which are methylated, and the effects of ammonium acetate and pH) of adenovirus-12-induced hamster tumor, normal hamster liver, and normal hamster muscle-connective tissue was studied. Enzyme extracts from the virus-induced tumor and the normal tissues were active on both *Escherichia coli* tRNA and yeast tRNA substrates although the degree of methylation was greater with *E. coli* tRNA. The total activity recovered was higher with the virus-induced tumor extracts (in which 1-methyladenine, 3-methyladenine, and N^6 -methyladenine bases were produced) than in extracts from muscle-connective tissue (3-methyladenine and an unidentified pyrimidine base) or from liver (1- and 3-methyladenine). Muscle-connective tissue extracts yielded both the 3-methyladenine and the unidentified base from *E. coli* tRNA at a pH of 7.0 but only the 3-methyladenine at a pH of 8.5; the same extracts yielded both 3-methyladenine and the unidentified bases from yeast tRNA at a pH of 7.0 and only the 3-methyladenine at a pH of 8.5. Ammonium acetate (480 $\mu\text{mole}/2\text{ ml}$) did not affect the bases methylated but increased the total activity recovered.

1050 THE EFFECT OF IMMUNIZATION ON THE RATE OF GROWTH OF ADENOVIRUS TYPE 12-INDUCED SARCOMA IN HAMSTERS. (Rus.) Ageyenko, A. I. (P. A. Herzen Res. Inst. Oncol., Moscow, USSR), V. T. Timofeyev, I. S. Bashkayev and E. Sh. Vardosanidze. *Vop Onkol* 16(10):64-66, 1970.

The effect of immunization on the growth of human adenovirus type 12-induced sarcoma in hamsters was studied. Antigens were obtained by subjecting sarcomatous tissue homogenates to 1) freeze-thawing, 2) ultrasonic treatment with or without addition of Freund's adjuvant or 3) heating at 56°C , and inoculating 5-7 hamsters 4 times at weekly intervals. Additional groups were treated with fresh homogenate or supernate, with normal hamster tissue homogenates (liver, spleen, muscle) or with Freund's adjuvant alone. Tumor producing amounts of trypsin-treated transplantable sarcomatous cells (9.5×10^6 or 19×10^6) were inoculated 10 days after the last immunization into 4 axillary sites and animals were sacrificed 2 wk later. Transplantability was 100%

in all the experimental animals. Immunization with both intact and treated homogenates, normal tissues and Freund's adjuvant stimulated tumor growth. The stimulation coefficients expressed in relative weights of total tumor tissue as compared to those developed in control (nonimmunized) hamsters were 3.5-4.7 in case of homogenates subjected to freeze-thawing, 5.3 in case of ultrasound treatment with addition of Freund's adjuvant, 3.8 when the homogenate was exposed to ultrasound only, 4.8 in case of normal tissue homogenates and 3.6 in the case of inoculation Freund's adjuvant only, when hamsters were injected with 19×10^6 tumor cells. No such effects were noticed in hamsters inoculated with homogenates heated at 56°C and then injected with 9.5×10^6 tumor cells. Massive inoculation with tumor tissue (19×10^6) seemed to produce immunosuppressive effects. The role of stimulation of tumor growth by immunization is still an open question in carcinogenesis.

- 1051 INTEGRATION OF THE DEOXYRIBONUCLEIC ACID OF ADENOVIRUS TYPE 12 INTO THE DEOXYRIBONUCLEIC ACID OF BABY HAMSTER KIDNEY CELLS. (E.) Doerfler, W. (Rockefeller U., New York, N. Y.). *J Virol* 6(5):652-666, 1970.

This study demonstrates the integration of viral DNA of adenovirus type 12 (Ad12) into cellular DNA of baby hamster kidney cells through covalent linkage. Adsorption of ^3H -Ad12 to baby hamster kidney cells occurred more efficiently at low concentrations with release of 82% of the ^3H activity that was cell associated being recovered in the medium at the end of 2 hr. The parental viral label hybridized predominantly to viral DNA and later to cellular DNA with a 25 to 1,380-fold higher value in infected cells as compared to uninfected control cells. Integration values are calculated to be 5-55 Ad12 DNA equivalents per cell, with only slightly lower values in the presence of cytosine arabinoside, cycloheximide and actinomycin D, indicating that DNA replication is not necessary for integration to occur.

- 1052 ADENOVIRUS TYPE 2-SIMIAN VIRUS 40 HYBRID POPULATION: EVIDENCE FOR A HYBRID DEOXYRIBONUCLEIC ACID MOLECULE AND THE ABSENCE OF ADENOVIRUS-ENCAPSIDATED CIRCULAR SIMIAN VIRUS 40 DEOXYRIBONUCLEIC ACID. (E.) Crumpacker, C. S. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), M. J. Levin, W. H. Wiese, A. M. Lewis, Jr. and W. P. Rowe. *J Virol* 6(6):788-794, 1970.

Adenovirus type 2 (Ad2) and simian virus 40 (SV40) DNA components of the hybrid population plaque variant high efficiency yielder (Ad2⁺HEY) were studied by equilibrium density centrifugation, and nucleic acid hybridization (with the virus-specific complementary RNA synthesized *in vitro*) and supercoiled SV40 DNA (form I) were investigated with alkaline sucrose gradients. The Ad2⁺HEY population contained a recombinant genome composed of Ad2 and SV40 DNA linked together within the same molecule; the failure of alkaline denaturation to

separate the components indicated a covalent linkage. Alkaline sucrose gradients of a mixture of ^{32}P -labeled SV40 DNA and ^3H -labeled Ad2 DNA revealed the broad peak expected for the denatured linear duplex molecule (Ad2 DNA) and 2 peaks for the SV40 DNA (the form I component and a mixture of forms II and III), while a mixture of ^{32}P -labeled Ad2⁺HEY DNA and ^3H -labeled Ad2 DNA revealed no SV40 DNA form I component. The DNA from the Ad2⁺HEY population apparently consists of nonhybrid Ad2 DNA and an Ad2-SV40 hybrid DNA.

- 1053 ENHANCEMENT OF ADENOVIRUS PLAQUE FORMATION ON HeLa CELLS BY MAGNESIUM CHLORIDE. (E.) Williams, J. F. (Inst. Virol., Glasgow, Scotland). *J Gen Virol* 9(3):251-255, 1970.

The effect of magnesium chloride on plaque-formation by adenoviruses in infected cultures of HeLa cells was investigated. Magnesium chloride in amounts ranging from 12-50 mM were added to cultures, with the result that adenovirus plaques began to appear in cultures 2-3 days earlier than normally; maximum plaque counts were also attained 2-3 days earlier than normally. In cultures supplemented with 25 mg magnesium chloride, 7 plaques were counted/50 mm petri dish on day 4, with maximal counts (50 plaques) falling on days 10-12. Optimal amounts of magnesium chloride for plaque-formation enhancement were between 25-30 mM; numbers of plaques began to decline when magnesium chloride supplements exceeded 30 mM. To determine whether the increased plaque-formation brought about by magnesium chloride was due to increase in viral yield at high magnesium chloride concentrations, infectivities were measured for intracellular and extracellular virus in cells infected with adenovirus at input multiplicities ranging from 0.05-5 plaque-forming units/cell. At low multiplicities of infection, levels of extracellular virus were 10-30-fold higher in cultures containing 25 mM of magnesium chloride, while levels of intracellular virus were not affected. Apparently, the effect of magnesium chloride supplement on plaque formation is due to an increase in the rate of virus release from infected cells.

- 1054 IMMUNOLOGICAL BASIS OF THE ADENOVIRUS 8-9 CROSS-REACTION. (E.) Hierholzer, J. C. (Ctr. Dis. Control, Atlanta, Ga.) and W. R. Dowdle. *J Virol* 6(6):782-787, 1970.

Cross-reactivity between the dodecon component purified 304- to 362-fold (fluorocarbon extraction, calcium phosphate batch chromatography, and ion exchange chromatography) and the hexon component purified 230- to 240-fold (erythrocyte adsorption, ion exchange chromatography, and exclusion chromatography) of adenovirus types 8 and 9 was studied. A bilateral but predominantly one-sided cross relationship existed between dodecons of types 8 and 9 in hemagglutinin inhibition tests with type 9 reacting equally well against type 8 (2560 titres) or type 9 (2560) antigens while type 8 reacted significantly less with type 9 antigen (40) than with the homologous antigen (2560). Dodecons and hexons

both types exhibited some neutralizing activity (0-80), and combining anti-dodecon and anti-hexon sera or producing antisera against a mixture of dodecon and hexon components produced neutralizing sera identical to those against crude virus. Dodecons and hexons of each type apparently shared at least 1 antigenic determinant (on the vertex hexamer). Complement fixation, neutralization, and immunodiffusion demonstrated group- and type-specific determinants in the hexon components.

5 TRANSPLANTATION IMMUNITY FOLLOWING IMMUNIZATION WITH EXTRACTS OF ADENOVIRUS 12

TUMOR CELLS. (E.) Potter, C. W. (Lodge Moor Hosp., Sheffield, England) and J. S. Oxford. *Int J Cancer* 5:410-414, 1970.

Induction of transplantation immunity by immunization with cells from tumors induced in mice with adenovirus 12 was investigated. Tumor extracts were prepared from transplanted adenovirus 12-induced tumors of mice and hamsters by freezing and thawing and centrifugation at 100,000 x g for 1 hr; the extracts were filtered through Millipore filters. CBA strain mice immunized by a s.c. injection of 0.1 ml of the adenovirus-induced tumor extract were challenged with 5×10^5 viable tumor cells 1, 2, or 3 wk later. No immunity was conferred by tumor cells in mice challenged 1 wk after immunization (95-100% of mice developing tumors); however, a significant reduction in tumors was seen in mice challenged 2 and 3 wk after immunization, immunized in these categories developing tumors in 70-100% of cases. Mice immunized with 3 doses of filtered tumor cell extract and challenged with viable tumor cells developed tumors in 3/20 cases, while mice immunized with antigen extracts from normal CBA tissue developed tumors upon challenge in all cases. Mice immunized with antigen extracts from transplanted hamster tumors induced by SV40, chick embryo lethal orphan virus, and adenovirus showed no immunity to tumor development on challenge with tumor cells. Apparently, a soluble extract of adenovirus 12 tumor transplantation antigen is present in tumors induced in CBA mice by adenovirus 12.

6 STUDIES OF THE ENHANCEMENT OF AN ADENOVIRUS ASSOCIATED VIRUS BY HERPES SIMPLEX VIRUS.

(E.) Blacklow, N. R. (Natl. Inst. Allergy Infect. Dis., 1. Inst. Hlth., Bethesda, Md.), R. Dolin and M. D. Hagan. *J Gen Virol* 10(1):29-36, 1970.

The interaction between herpes simplex virus type I and adenovirus-associated virus type I (AAV) was investigated; quantitative kinetic procedures were employed to examine herpes virus replication and the activity of AAV and herpes virus-infected cells to produce AAV antigen detectable by immunofluorescent tests. Cultures of Hep-2 cells inoculated with AAV alone failed to produce immunofluorescent antigen, but when co-infected with AAV and herpes simplex virus, the cells showed AAV specific antigen. Between 6-18 days after infection, titers of herpes simplex virus were from $2.5-6.5 \log_{10}$ TCID₅₀/ml. AAV fluorescent

cells increased from 0.03% to 5.0% 6-12 hr after infection. Dose response studies showed that a single infectious AAV particle and a single infectious herpes simplex virus particle were sufficient to initiate AAV antigen synthesis. In co-infected cultures, AAV antigen was produced before herpes simplex virus. When arginine was removed from co-infected cultures, it was found that herpes simplex virus was not produced, while AAV antigen production proceeded as in arginine-positive cultures, but at a slower rate, the percentage of AAV fluorescent cells at 12 hr postinfection being 0.05%. Preinfection with herpes simplex virus lengthened the 6 hr latent period for AAV antigen production. When co-infected cultures were treated with cytosine arabinoside AAV antigen production was abolished.

1057 PATHOGENICITY STUDIES IN RABBITS, HAMSTERS, MICE AND EMBRYONATED EGGS WITH HERPES T VIRUS VARIANTS. (E.) Daniel, M. D. (Harvard Med. Sch., Southboro, Mass.) and L. V. Melendez. *Arch Gwa Virusforsch* 32(1):45-52, 1970.

The pathogenicity and antigenicity of a large plaque variant (LPV) and a small plaque variant (SPV) of herpes tumor virus was investigated in mice, hamsters, rabbits and embryonated chicken eggs. Both variants formed pocks when inoculated in embryonated eggs; LPV formed larger pocks than SPV, and the LPV-induced pocks appeared 2 days after inoculation, while SPV-induced pocks appeared after day 3. LPV intracerebral inoculation was 100% fatal in weaned and adult mice, death ensuing in 3-7 days. Seventy percent mortality was observed in weaned mice inoculated i.m. with LPV; mortality declined to 16% in mice inoculated at 7 wk-of-age. SPV proved fatal only to 1-day-old mice; intracerebral inoculation of weaned and adult mice was not fatal. Mice inoculated with SPV showed a 90% survival when challenged with LPV inoculations 21 days later. LPV was 100% lethal in 4-day-old hamsters and 93% lethal in weaned animals with intracerebral inoculation; it was not lethal when inoculated by s.c., i.m., or i.p. routes. SPV was lethal to 1 and 2-day-old hamsters by the intracerebral route but with inoculation at 4 days, survival rose to 56% and to 100% at 3 wk. Corneal scarification and instillation of 2 drops of LPV in rabbits produced acute conjunctivitis and keratitis by 3 days postinfection. SPV administered similarly failed to produce ocular lesions. LPV was more antigenic than SPV and produced higher antisera titers; sera from animals inoculated by corneal infection produced high antibody titers in 14 days, while the i.p. inoculation was slower in producing antibodies.

1058 RNA SYNTHESIS IN CELLS INFECTED WITH HERPES SIMPLEX VIRUS: III. ABSENCE OF VIRUS-SPECIFIC ARGINYL- AND SERYL-tRNA IN INFECTED Hep-2 CELLS. (E.) Morris, V. L. (Dept. Microbiol., U. Chicago, Ill.), E. K. Wagner and B. Roizman. *J Molec Biol* 52(2):247-263, 1970.

Experiments were designed to test the ability of herpes simplex virus to specify its own arginine- or

serine-specific transfer RNA in human epidermoid carcinoma no. 2 cells (HEp-2) utilizing co-chromatography and hybridization competition tests. Arginyl-tRNA reached a maximal level after 15 min at 37°C and remained unaltered for at least 15 additional min, showing that little or no RNase was present. Hydrogen ion concentration and the ratio of magnesium ion:ATP did not alter populations of tRNA charged with arginyl-tRNA synthetase. No differences in elution profiles of arginyl-tRNA extracted from infected and uninfected cells determined from inspection of $^3\text{H}/^{14}\text{C}$ ratios was noted. Chromatographic properties of seryl-tRNA were indistinguishable from those of the corresponding tRNA's of uninfected cells. Approximately 2 moles of purified 4 S RNA of molecular wt 25,000 daltons extracted from infected cells hybridized with 1 mole of viral DNA; the annealed nucleotide sequences were homologous to those found in nuclear RNA of molecular wt 50,000 daltons or higher. Arginine-specific or serine-specific tRNA could not be shown to anneal to viral DNA. If viral arginine- and serine-specific tRNA are coded in HEp-2 cells, they are made in amounts insufficient to be detected.

- 1059 LETHAL RETICULOPROLIFERATIVE DISEASE INDUCED IN *CEBUS ALBIOFRONS* MONKEYS BY *HERPESVIRUS SAIMIRI*. (E.) Melendez, L. V. (Harvard Med. Sch., Southboro, Mass.), R. D. Hunt, M. D. Daniel, C. E. O. Fraser, F. G. Garcia and M. E. Williamson. *Int J Cancer* 6(3):431-435, 1970.

A reticuloproliferative disease induced in monkeys by *Herpesvirus saimiri* was investigated in 4 ring-tail cinnamon monkeys. Monkeys were injected i.m. with 0.5 ml of undiluted Cebus isolate virus; 6 months later undiluted *H. saimiri* were inoculated into the monkeys (0.5 ml, i.m.). All monkeys died between 18-20 days after *H. saimiri* injection. Sera were assayed for viral antibodies and no antibodies to either Cebus isolate virus or *H. saimiri* were found. No cytopathic effect was observed in owl monkey cultures inoculated with liver and kidney samples from monkeys injected with Cebus isolate virus and *H. saimiri* virus. A cellular infiltrate was found at autopsy in the liver, lung, thymus and lymph nodes of each monkey and in the spleen and pancreas of certain of these animals. The infiltrate was composed primarily of round, polygonal to fusiform cells with leptochromatic nuclei and eosinophilic cytoplasm, and were thought to be reticulum cells. Multinucleated giant cells were occasionally observed in the reticulum cell sheets in the thymus. These reticulum cell infiltrates resembled reticulum cell sarcoma. It appeared that the reticuloproliferative disease in these monkeys was induced not by Cebus isolate virus but by *H. saimiri*.

- 1060 TEMPERATURE-SENSITIVE MUTANTS OF HERPES SIMPLEX VIRUS. (E.) Schaffer, P. (Baylor Coll. Med., Houston, Tex.), V. Vonka, R. Lewis and M. Benyesh-Melnick. *Virology* 42(4):1144-1146, 1970.

Human embryonic lung fibroblast cultures were infected with wild-type herpes simplex virus and in-

cubated with the mutagen 5-bromodeoxyuridine in concentrations of 0.3-5.0 µg/ml culture for 48 hr. Treated cultures were frozen and thawed 3 times and centrifuged, and the supernatants were stored at -90°C. These mutagenized viral stocks were seeded on human embryonic lung fibroblast monolayers, and the growth increments of plaques were observed. Plaques which did not increase in size during 24 hr were regarded as potential mutants. Of 708 plaques isolated, 22 were shown to have greatly decreased capacity for growth at 40° when compared to wild-type virus. Wild-type virus showed virus titers of 4.2×10^7 plaque-forming U at 40°, while representative mutants had titers of 1.0×10^2 and 4.5×10^2 . All mutants except one exhibited multiplicity-dependent leakiness, and all were significantly neutralized by herpes simplex virus antiserum.

- 1061 GENITAL HERPESVIRUS HOMINIS TYPE 2 INFECTION: AN EXPERIMENTAL MODEL IN CEBUS MONKEYS. (E.) Nahmias, A. J. (Emory U. Sch. Med., Atlanta, Ga.), W. T. London, L. W. Catalano, D. A. Fuccillo, J. L. Sever and C. Graham. *Science* 171(3968):297-298, 1971.

Attempts were made to infect the genital organs of female monkeys of 3 species with herpesvirus hominis type 2. The virus was originally obtained from a female patient and had undergone 3 or 4 passages in tissue cultures of rabbit kidney. Cotton pellets were impregnated with undiluted virus (titers of $10^{5.5}$ - $10^{6.5}$ TCID₅₀) which were implanted in the vaginal vault. Infections could not be produced by this method in squirrel monkeys or rhesus monkeys; however 10 cebus monkeys (*Cebus albifrons*) were successfully infected. Virus could be detected by immunofluorescence in cervico-vaginal swabs from 3-16 days after inoculation in 3 monkeys. All monkey had inflamed vaginas and cervixes, and 7 had herpetic like vesicles or ulcers on the vulvas. Four monkeys developed perineal and finger lesions from which virus could be recovered. Genital reinfection attempts with the same herpesvirus hominis strain were successful in 3 monkeys. All monkeys had neutralizing viral antibody in the serum. The infection of cebus monkey by herpesvirus hominis may be a valuable model for human infection by this virus.

- 1062 HERPESVIRUS ANTIGENS ON CELL MEMBRANES DETECTED BY CENTRIFUGATION OF MEMBRANE-ANTIBODY COMPLEXES. (E.) Roizman, B. (Dept. Microbiol. U. Chicago, Ill.) and P. G. Spear. *Science* 171(3968):298-300, 1971.

The binding of antiviral antibodies to cell membranes was investigated in herpes viruses. It was found the glycoproteins specified by herpes viruses bind to cell membranes and appear in the virion envelope. When antiviral antibodies were incubated with purified smooth membranes of human epidermoid carcinoma cells infected with virus, an increase was observed in the density of the membranes which was revealed in sucrose density gradient centrifugation. While the densities of untreated membranes were 1.08 g/cm³, densities of cell membranes treated with antibodies were as high as

1.6 g/cm³. Antiviral antibody did not increase the density of uninfected cell membranes, and saline and normal rabbit serum did not change the densities of infected or of uninfected cell membranes. It was suggested that viral antigens, probably the glycoproteins specified by the virus, were located on the surface of infected cell membranes, and were bound strongly enough to withstand the membrane isolation procedures.

1063 DETECTION IN CHICKEN AND HUMAN SERA OF ANTIBODY AGAINST HERPES TYPE VIRUS FROM A CHICKEN WITH MAREK'S DISEASE AND EB VIRUS DEMONSTRATED BY THE INDIRECT IMMUNOFLUORESCENCE TEST. (E.) Iwamoto, M. (Res. Inst. Microbial Dis., Osaka U., Japan), K. Ono, S. Tanabe, T. Doi and S. Kato. *Biken J* 13(3): 205-212, 1970.

Antibodies to chick herpes type virus antigen were found in sera from chickens with Marek's disease, healthy chickens and healthy humans; anti-Epstein-Barr virus antibody titers in sera from chickens with Marek's disease and in healthy humans were also examined. Herpes type virus antigens were prepared in duck embryo fibroblasts infected with herpes type virus from a chicken with Marek's disease. High antibody levels against chick herpes type virus antigens were found in sera from chickens with viremia of chick herpes type virus, in sera from chickens with Marek's disease, and in sera from chickens inoculated with herpes type virus. All sera from chicks in these conditions aged from 0-10 days had antibodies, while chicks aged from 11-30 days had lower incidences of antibody. Antibody levels increased in chicks aged 30-61 days. Antibody titers in the older chicks were at levels greater than or equal to 1:640. However, sera from chicks free of specific pathogen and negative COFAL tests had low incidences of antibody; sera from 11 specific pathogen-free chicks raised in vinyl isolators showed no antibody. Most sera prepared from healthy human subjects contained antibody activity against chick herpes type virus. The anti-Epstein-Barr virus antibody titers in sera from chickens were also tested using indirect immunofluorescent techniques; some chick sera were Epstein-Barr virus antibody-positive, but titers of antibody were not so high as titers of herpes type virus antibody. Antibodies to herpes type virus in sera from 7-18-day-old chicks may have been derived from maternal antibody stores.

1064 POLYPEPTIDES OF AVIAN RNA TUMOR VIRUSES: I. ISOLATION AND PHYSICAL AND CHEMICAL ANALYSIS. (E.) Bolognesi, D. P. (Max Planck Inst. Virus. Res., Tübingen, Germany) and H. Bauer. *Virology* 42(4):1097-1112, 1970.

The protein components of avian myeloblastosis virus were extracted with phenol and SDS and examined electrophoretically. Major components with molecular wt ranging from 13,000-28,000 and minor components with molecular wt well in excess of these were found. Four major bands were detected by specific staining and were present in viruses from subgroups A and B. A component protein of molecular wt 15,000 showed unusual staining properties with amido black stain, but incorporated radioactive amino acids poorly.

Another component (23,000 molecular wt) tended to aggregate, but this tendency was eliminated by treatment with dithiothreitol. The component proteins of higher molecular wt included one (115,000 molecular wt) which was associated with material which could be stained with polysaccharide and which was strongly labeled with ¹⁴C-glucosamine. A similar component was found in preparations which contained the type-specific antigen of the avian myeloblastosis virus.

1065 POLYPEPTIDES OF AVIAN RNA TUMOR VIRUSES: II. SEROLOGICAL CHARACTERIZATION. (E.)

Bauer, H. (Max Planck Inst. Virus Res., Tübingen, Germany) and D. P. Bolognesi. *Virology* 42(4):1113-1126, 1970.

The antigenicity of various protein components of avian myeloblastosis virus were investigated following extraction of virus with phenol and SDS and electrophoresis of the protein components on acrylamide gels. This process did not result in any significant loss of group-specific complement-fixing antigenicity, and the antigenic properties of the major viral polypeptides could be ascertained. Four major components were detected in complement fixation tests with group-specific rabbit and group-specific hamster antisera. The different protein components appeared to be immunologically distinct, and their differences were further accentuated in agar gel double diffusion tests. Viral components 1 and 2 were immunogenically weak, while components 3 and 4 were more antigenic. Component 4 appeared to be identical to a material shown previously to have the properties of a group-specific antigen. Much of the type-specific antigenicity was lost in the treatment of the virus; however, it was possible to test various fractions remaining after electrophoresis. Most of the virus envelope antigen was found in the region of the main glycoprotein component of the virus, but no correlation could be demonstrated between this antigenic activity and the polysaccharide staining material.

1066 DIFFERENCES BETWEEN THE RIBONUCLEIC ACIDS OF TRANSFORMING AND NON-TRANSFORMING AVIAN TUMOR VIRUSES. (E.) Duesberg, P. H. (Dept. Molec. Biol., U. California, Berkeley) and P. K. Vogt. *Proc Nat Acad Sci* 67(4):1673-1680, 1970.

Differences in the RNAs of a transforming avian sarcoma virus B77 and its nontransforming derivatives both in their native forms and after heat dissociation into subunits are reported; the nontransforming viruses were isolated after UV irradiation of B77. The viruses were grown in suspension cultures of myeloblasts from leukemic chickens, and viral RNA was labeled with ³H-uridine and ³²P-H₃PO₄. The RNAs of the nontransforming virus were found to migrate slightly faster than RNA of B77 with gel electrophoresis. Electropherograms of the heat-dissociated RNAs demonstrated both classes of RNA subunits *a* and *b* in B77, but in 2 of the nontransforming viruses, NT B77 clone 5 and NT B77 clone, the class *a* subunit was absent. The absence of class *a* RNA may be related to the inability of these viruses to transform chick embryo

fibroblasts in tissue culture, or its presence may be merely the consequence of the transformed state of the cell.

- 1067 INABILITY TO PREDICT MAMMARY TUMORIGENESIS IN STRAIN A MICE FROM PRESENCE OF MAMMARY TUMOR VIRUS OR ANTIGEN IN THE MILK. (E.) Heston, W. E. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), W. T. Hall, G. Vlahakis, J. Charney and D. H. Moore. *J Nat Cancer Inst* 45(5):937-940, 1970.

The correlation of development of mammary tumors and the presence in mammary milk of mammary tumor virus (MTV) and of MTV antigen was investigated in breeding female mice of the A/He strain in which the incidence of mammary tumors is about 40%. The presence of MTV in milk was tested for by an alveolar nodule test and MTV antigen by a microimmunodiffusion test. Full agreement was not found between the results of the MTV tests and the results of the MTV antigen tests. Of 35 tested samples, 18 were MTV antigen-positive and 17 were antigen-negative. Virus-presence tests were run only on 19 samples; of these samples 9 were shown to contain virus antigen and 10 did not contain virus antigen. Fourteen of the 19 samples contained virus, however, producing hyperplastic alveolar nodules at milk dilutions of from 10^{-1} - 10^{-4} . Eight of the virus-containing samples were also antigen-positive; of the 5 samples which did not contain virus, 3 were also antigen-negative, but 2 were antigen-positive. The presence in milk of virus and/or antigen could not be used to predict subsequent development of mammary tumors. Twelve of the tested mice developed tumors (34%). Seven of these were virus antigen-negative, and 9 of the antigen-positive mice remained tumor-free for the duration of the experiment. Seven of the mice which developed mammary tumors were virus-positive, but 2 females which developed tumors were virus-negative. Seven virus-positive mice failed to get tumors. Apparently, mammary tumorigenesis in this mouse strain is determined by factors other than the presence of MTV in the milk.

- 1068 DISSOCIATION BETWEEN CELL CONVERSION INDUCED BY MOUSE SARCOMA VIRUS AND PRODUCTION OF INFECTIOUS VIRUS. (E.) Guillemain, B. (Hosp. St. Louis, Paris, France), J. Laumond, C. Godard and M. Boiron. *J Gen Virol* 10(1):91-93, 1970.

The dependence on virus multiplication of cell conversion by mouse sarcoma virus isolate (MSV) was investigated by treating infected cell cultures with 5-fluorouracil to block this multiplication. Monolayers of mouse cells were infected with MSV, and 5-fluorouracil was added to the cultures in differing concentrations. The number of foci present decreased as the concentration of 5-fluorouracil increased; at a concentration of 0.0125 $\mu\text{g/ml}$, the percent of foci counted was about 80%, while at concentrations of 5-fluorouracil of 0.8 $\mu\text{g/ml}$, the percent of foci counted was 0.5%. In this experiment, the multiplicity of introduction of the virus was 2×10^{-4} FFU/cell and the amount of 5-fluorouracil needed to give 99.9% focus inhibition was about 1.0 $\mu\text{g/ml}$. For higher multiplicities of introduc-

tion, the dose of 5-fluorouracil needed to fully inhibit focus formation was higher. At doses of 25 μg of 5-fluorouracil cell multiplication was inhibited, and the rate of nucleic acid synthesis was reduced to 10% of normal and was evenly distributed between RNA and DNA. These findings suggest that cell conversion induced by MSV is related to an effect which occurs before replication of the virus.

- 1069 ENHANCEMENT OF MURINE SARCOMA VIRUS (MOLONEY) INFECTION IN MICE BY GUAROA VIRUS. (E.) Turner, W. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), W. Gibson and M. A. Chirigos. *Cancer Res* 30(11):2645-2651, 1970.

Temporal studies are presented in this report which show the potentiating effects of dually infecting mice with murine sarcoma virus (Moloney) and Guaroa virus. Mice were inoculated by various routes with Guaroa virus prior to or simultaneously with intramuscular inoculation of murine sarcoma virus (Moloney) and the time intervals noted with respect to increased incidence of death. Potentiation was most pronounced in mice inoculated with Guaroa virus three days prior to and simultaneously with murine sarcoma virus (Moloney) and resulted in earlier tumor deaths. Guaroa virus showed no effect on the humoral or cellular immune response nor did it produce significantly different titers of interferon from noninfected mice. The mechanism whereby Guaroa virus, a nononcogenic arbovirus, enhances murine leukemia in mice is not yet known.

- 1070 RESCUE OF MURINE SARCOMA VIRUS GENOME IN MIXED CULTURES OF "NON-PRODUCER" HAMSTER TUMOUR CELLS AND HELPER VIRUS CARRIER CELL LINES. (E.) Chang, S. S. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), R. V. Gilden and R. J. Huebner. *J Gen Virol* 10(1):107-110, 1970.

The rescue of the Moloney isolate of murine sarcoma virus (MSV) from non-producer hamster tumor cells (HT-1) by cocultivation with various murine leukemia virus (MLV)-carrier cells of mouse and hamster origin (F4 and F5 from Rauscher pseudotype MSV-transformed foci of mouse embryo cells, the Walkersville cell line (WH-1) from mouse tumor carrying a wild type MLV, and the RHT cell line from RLV-transformed hamster embryo cells) is described. Co-cultivation of HT-1 and F4 resulted in MSV recovery in more than 20 attempts, while mixed cultures of HT-1 with F5, WH-1, or RHT cells yielded MSV only once or twice in 3-5 attempts. The differences in rescue efficiency were related to the infectivity of the helper viruses for mouse embryo cell (except with F5). A 100-fold decrease in MSV rescue resulted from each 10-fold decrease in the number of F4 cells, and excess (2×10^5) HT-1 cells decreased the yield of MSV. A reproducible growth curve for MSV retrieval was obtained with optimal numbers of HT-1 (8×10^4 cells) and F4 (8×10^5 cells).

1 STRUCTURAL PROTEINS OF KILHAM RAT VIRUS.
(E.) Salzman, L. A. (Natl. Inst. Allerg.
ect. Dis., Natl. Inst. Hlth., Bethesda, Md.) and
L. White. *Biochem Biophys Res Commun* 41(6):1551-
56, 1970.

The component proteins of the Kilham rat virus were
investigated and described. Virus was cultured in
rat nephroma cell line at an input multiplicity
5 plaque-forming U/cell. Viral proteins were
separated by the addition to the culture of a mixture
of ^3H - or ^{14}C -L-amino acids, and protein subunits
were separated by electrophoresis on polyacrylamide
gels and by agarose gel filtration in 6M guanidine-
HCl. Electrophoresis of radioactive Kilham virus
proteins showed 3 major bands of radioactivity (A,
B, and C), which were found to have molecular wt of
100,000 daltons, 62,000 daltons and 55,000 daltons,
respectively. Component A made up 13.1% of the total viral
protein, component B made up 75.5%, and component C,
11.4%. Hemagglutination tests revealed that compo-
nent B showed strong hemagglutination activity as well
as strong hemagglutination inhibition. It was con-
cluded that component B was probably a capsid pro-
tein.

2 IMMUNOLOGICAL STUDIES ON A "SPONTANEOUS-
LY" TRANSFORMED CELL LINE OF SWISS MOUSE
EMBRYONAL FIBROBLASTS: A POSSIBLE VIRAL ONCOGENESIS.
(E.) Vernekar, S. D. (Cancer Res. Inst. Tata Mem.
Hospital, Parel, Bombay, India), S. G. Gangal and K. J.
Sinha. *Indian J Exp Biol* 8(1):7-10, 1970.

Culture of mouse embryo fibroblasts which had un-
dergone spontaneous malignant transformation was
examined for antigens to virus. The cell line,
maintained as a plasma clot culture, produced tumors
in 73% of mice as early as the 15th passage *in vitro*.
Cells were thought to possess 100% tumorigenicity
at an early stage. Accordingly, the cultures were
tested with antisera prepared from a heterologous
rabbit serum in order to confirm the possibility
of a viral etiology for the malignant transformation.
Tumor and cell extracts from the test cultures re-
acted well in complement fixation tests with anti-
virus; antigens were selected in such a way as to
exclude known cross-reactivities. High complement
fixing titers were obtained with tumor extracts test-
ed with unabsorbed rabbit antisera (titers of 126).
High complement fixing titers were also observed
in tumor extract cells were tested with rabbit
anti-adenovirus 12 antisera (titer of 512). Anti-
virus reactions with the heterologous rabbit anti-
sera were considered to be specific for an antigen
of the transformed malignant cells not found in nor-
mal tissue of the species and strain. The findings
presently suggested an unknown viral infection as
the cause of malignant transformation in the test
cell system.

3 PROPAGATION IN HUMAN CELLS OF A FILTER-
ABLE AGENT FROM THE ST FELINE SARCOMA.
(E.) Chang, R. S. (Dept. Med. Microbiol., U.
California, Davis), H. D. Golden and B. Harrold.
Virology 6(5):599-603, 1970.

A filtrate prepared from Snyder-Theilen feline sar-
coma (ST feline sarcoma) was propagated in human
fibroblast cultures from embryonic or sarcomatous
tissues. Seven of the 19 human cell lines tested
showed morphological alteration and released focus-
forming activity, and 2 lines showed alterations
but did not release focus-forming activity; 11 cell
lines neither showed morphological alterations nor
released focus-forming activity. A cell line de-
rived from an osteosarcoma at the 21st passage con-
sistently showed the most extensive morphological
changes on inoculation of feline cell cultures.
Altered cells were enlarged and hyper-refractile;
they stained intensely with hematoxylin. These
cells did not form visible foci, nor did they assume
a criss-cross pattern. Altered cells did not
divide and were motile. Cells derived from osteo-
sarcomas below the 10th passage level consistently
failed to show focus-forming activity. No inter-
feron activity was detected in the sarcoma filtrate
and in culture fluids from 8 cell lines. Fibro-
sarcoma was induced in newborn kittens by inocu-
lation with the fluid from 2 human fibroblast cul-
tures which had been treated with ST feline sarcoma
filtrate 4 and 14 wk before.

1074 INDUCTION OF PAPILLOMAS IN RABBITS WITH
NUCLEIC ACID EXTRACTS FROM Vx7 CARCINOMAS.
(E.) Ito, Y. (Aichi Cancer Ctr., Nagoya, Japan).
Brit J Cancer 24(3):535-541, 1970.

The ability of nucleic acid extracts from transplanta-
ble carcinomas Vx2 and Vx7 (one of the series of
transplantable carcinomas of the Shope papilloma-
carcinoma sequence) to induce tumors in rabbits was
investigated. The Vx7 and Vx2 tumors had been main-
tained in domestic rabbits for 111 and 203 genera-
tions, resp. Vx2 carcinomas were more invasive than
Vx7 carcinomas in the donor rabbits, the former tu-
mor type showing metastases to the lymph nodes in
109 cases, and the latter tumor metastasizing to
this site in only 18 cases. Histologically, Vx7 tu-
mors were characteristically squamous cell type car-
cinomas, while Vx2 were entirely anaplastic. At 5-7
wk after administration of nucleic acid extracts
from Vx7 tumors to rabbits, papillomatous growths
arose at a number of inoculation sites; numbers of
papillomatous growths/number of inoculation sites
ranged from 12/84-6/84. The majority of tumors in-
duced by nucleic acid from Vx7 tumors regressed af-
ter a certain period of growth on the rabbits' skin.
One papilloma underwent malignant conversion to the
status of a squamous cell carcinoma in the course of
77 wk. Efforts to induce tumors with nucleic acid
preparations from Vx2 tumor were entirely unsucces-
ful. Efforts to detect Shope papilloma virus in nu-
cleic acid-induced tumors revealed only 1 possibly
virus-associated excrescence in 400 inoculation sites.

1075 SOME FEATURES OF VIRAL RETICULUM CELL
SARCOMA IN MICE. (Rus.) Bergolits, V. M.
(P. A. Herzen Res. Inst. Oncol., Moscow), V. S.
Ter-Grigorov and O. Ya. Moskvkina. *Vop Onkol*
16(9):53-58, 1970.

Several features of viral reticulum cell sarcoma (RS) were investigated in CC 57BR/Mv, C57BL/G, C3HA and BALB/C mice and in Wistar rats. Virus preparations such as cell-free tumor nodule extracts or heparinized plasma from leukemic mice with RS were used. Cytologically detectable early stages of RS were noticed in 53% of the CC57BR mice at 1-1.5 months following i.v. or i.p. injection of either preparation; advanced forms of RS seen at this time (20%) increased to 75% at 2-3 months. The presence of leukemogenic virus in the plasma of these mice was proved in 10^{-3} - 10^{-4} dilutions. Large amounts of viral particles, 140-150 m μ in diameter were prevalent in the intercellular spaces as seen by electron microscopy. The possibility of RS virus cultivation *in vitro* (segments of RS tissue in embryonic tissue-containing plasma and medium 199 plus 10% bull serum) was proved by i.v. inoculation with cell-free liquid phase after 11 and 47 days of culture which induced leukemia in 2 of 12 mice 35 days following contamination and RS in 4 of 4 mice killed 4 months after inoculation, resp. Transmittance of RS from CC57BR mice (by cell-free extract inoculation or cell transplants) was possible only into C57BL/6 mice having a closely related genotype with the CC57BR mice; however, the occurrence of RS appeared irregular and after 5-14 month-long latency periods. Inoculation of 16 newborn Wistar rats with RS material induced leukemia in 1 rat of the 16-19 month-old animals. Suppression of resistance to RS virus was achieved with Freund's adjuvant in the BALB/c and CC57 W lines. Group-specific antigen was found to be present in RS in amounts similar to those found in Gross-, Rauscher-, Friend- and Moloney-virus-induced leukemias. Attempts to induce antiRS immunity in CC57BR mice by preliminary inoculation with low virus dosages failed; tumor growth stimulation took place instead. Mouse RS is concluded to be an appropriate model for experimental investigation.

- 1076 CHARACTERIZATION OF THE COMPLEMENTARY NUCLEAR RNA OF MURINE SARCOMA-LEUKEMIA VIRUS. (E.) Biswal, N. (Baylor Coll. Med., Houston, Tex.) and M. Benyesh-Melnick. *Virology* 42(4):1064-1072, 1970.

This study is an investigation into the sedimentation behavior of the viral RNA-nuclear RNA hybrids and the complementarity of the base composition of heat dissociated RNA (37 S) of murine sarcoma-leukemia virus hybridized with 32 P-labeled heat denatured nuclear RNA of cells infected with murine sarcoma-leukemia virus. Three distinct sedimenting species of RNA hybrids were formed, 18 S, 10.5 S and 4 S. The 18 S hybrid showed virus-specificity and an overall base composition similar to the viral RNA, indicating it may be a true specific product of hybridization of the viral RNA with its complement in the nucleus of the transformed cell. Murine sarcoma-leukemia virus RNA may possibly replicate like the RNA of nononcogenic viruses.

- 1077 RELATIONSHIP BETWEEN GROWTH RATE, CELL VOLUME, CELL CYCLE KINETICS, AND ANTIGENIC PROPERTIES OF CULTURED MURINE LYMPHOMA CELLS. (E.)

Cikes, M. (Karolinska Inst., Sch. Med., Stockholm, Sweden). *J Nat Cancer Inst* 45(5):979-988, 1970.

Mechanisms underlying the expression of H-2 and Moloney leukemia virus-induced surface antigens of murine lymphoma cells during the growth cycle were clarified through the use of indirect membrane immunofluorescence testing and complement-dependent antibody-mediated cytotoxic sensitivity testing. A rapid fall in cytotoxic sensitivity was shown in cells during the first 48 hr after seeding followed by a rise until 148 hr when a decline was again noted, with a similar pattern established for indirect membrane immunofluorescence reactivity. Cell volume of the whole population indicated a marked shift toward small cell populations between 48 and 148 hr, with the larger cells showing a growth rate higher than that of smaller cells. Life cycle analysis at different intervals during the growth cycle showed that variations in duration of population doubling time influenced the length of the G1 period mainly. Variations in expression of surface antigens on cultured cells during the growth cycle can be considered the result of limiting periods of synthesis of membrane antigenic receptors. Hence, variations in concentration of surface antigens on cultured mouse lymphoma cells may result from sequential repression and derepression of genes specifying the synthesis of cell-surface antigens.

- 1078 A STUDY OF THE ONCOGENIC AND INFECTIOUS FUNCTIONS OF ROUS SARCOMA VIRUS. (Fr.) Golde, A. (Fac. Sci. Orsay, France). *Bull Cancer* 57(2):195-216, 1970.

Oncogenic action and reproduction capability of Rous virus *in vitro* were investigated on chick embryo fibroblast cultures with various mutants of the Schmidt-Ruppin strain by varying the conditions of cell culture, promoting one or the other of the investigated functions. Two defective mutants of the Schmidt-Ruppin strain were obtained by exposure to 3000 kr of 60 Co emitting γ -radiations; one mutant had oncogenic properties but was unable to reproduce itself within the transformed cell culture, and the other was a noncarcinogenic mutant capable of reproduction. The neoplastic nature of the cells transformed by the oncogenic mutant was confirmed by their transplantability into eggs with 10 day-embryos; these cells did not release virions and were referred to as NP cells. The non-oncogenic mutant was referred to as NT gamma mutant and produced no morphological alterations in chick embryo fibroblasts. However, these virions contained a group specific (gs) antigen characteristic for avian oncogenic viruses. The occurrence of these 2 different mutants suggested that oncogenicity and reproduction were coded by different independent portions of the viral genome; it was postulated that the viral RNA molecule could be constituted of several independent subunits. Variations of culture conditions indicated that the infection and transformation efficacy of Schmidt-Ruppin and Bryan mutants was not cell age dependent. These properties seemed to be affected by the number of monocellular layers (degree of confluence)

the moment of infection. A cellular density of monolayers appeared to be the threshold when cell transformation would no longer occur, although infection and virion production were still possible. The factor of cellular density apparently did not affect infectivity and virion productivity but did inhibit the reading of the viral information needed to induce cell transformation.

79 ADENINE NUCLEOTIDE DEPENDENT ULTRASTRUCTURAL SURFACE ALTERATIONS IN TRANSFORMED BHK 21/13 CELLS. (Fr.) Torpier, G. (Inst. Pasteur, Lille, France) and L. Montagnier. *Int J Cancer* 6(3):529-535, 1970.

Adenine nucleotide-dependent surface cell alterations were studied by means of ruthenium red staining in BHK 21/13 cell cultures subjected to Rous or polyoma virus transformation. The cell clones were grown in glass bottles on ETC 10 media with 10% bactotryptose phosphate and 10% calf serum treated with 5 µg/ml of streptomycin. The role of nutritive factors was studied on Eagle BME media treated with 10% calf serum and 3 mg glucose/ml (basic media). The cell cultures transferred from the ETC 10 media were kept for 48 hr in the basic media until the end of their exponential growth before being subjected to ultrastructural investigation. Electron microscopy revealed a thick ruthenium red staining layer on the external surface of the cytoplasmic membrane in both normal and transformed BHK 21/13 cells; this layer was thicker in transformed cells grown wholly on ETC 10 media. In normal cells cultivated on basic media lacking bactotryptose for 48 hr before fixation, no differences were seen in the thick layer compared to the clones grown on ETC 10 media. Addition of ribosomal RNA (200 µg/l) or of pancreatic ribonuclease-hydrolyzed RNA or of adenine nucleotides such as adenosine 3'- or 5'-phosphate (300 µM/ml) produced considerable thickening of the ruthenium red staining layer in all transformed clones. UMP, CMP and GMP had no such effects. AMP had less effect in the presence of bactotryptose and no effect in the original BHK 21/13 clone. The mechanism of action of adenine nucleotides in modifying the cell surface may possibly be the same in all transformed cells; this mechanism seems to be associated with the initial changes related to transformation of these cell clones by the oncogenic viruses.

80 STUDIES ON NUCLEIC ACIDS IN ROUS SARCOMA VIRUS-INDUCED MOUSE ASCITES SARCOMA CELLS. DISTRIBUTION AND ELECTRON MICROSCOPY OF NUCLEIC ACIDS IN SUBCELLULAR FRACTIONS AND CIRCULAR DNA IN MITOCHONDRIAL FRACTIONS. (E.) Yamamoto, G. (Okayama U. School of Medicine, Japan) and T. Oda. *Acta Med Okayama* 25(3):287-302, 1970.

The distribution of nucleic acids in subcellular fractions (differential centrifugation) of mouse ascites sarcoma cells (SR-C3H) induced by Rous sarcoma virus and of normal C3H mouse liver was studied, and the extracted nucleic acids were examined by electron microscopy. The RNA/DNA ratios were 2.3 and 3.7 in the homogenates and 0.34 and 0.56 in the

nuclear fractions of SR-C3H cells and liver cells, resp. DNA and RNA contents of SR-C3H mitochondria (3.1 and 24 µg/mg protein, resp.) were higher than in liver mitochondria, but the mean value of the contour length of circular DNA molecules was smaller in SR-C3H mitochondria (4.88 µ) than in liver mitochondria (5.08 µ). Microsomal and supernatant fractions of both the SR-C3H cells and liver contained DNA equivalent to 3-6% of the RNA content; the SR-C3H supernatant fraction seemed particularly high in DNA content, and electron micrographs revealed fibrous linear structures (double-stranded nucleic acids) in the SR-C3H supernatant but not in the liver supernatant.

1081 DEOXYRIBONUCLEIC ACID POLYMERASE ASSOCIATED WITH ROUS SARCOMA VIRUS AND AVIAN MYELOBLASTOSIS VIRUS: PROPERTIES OF THE ENZYME AND ITS PRODUCT. (E.) Garapin, A. C. (Dept. Microbiol., U. California, San Francisco), J. P. McDonnell, W. Levinson, N. Quintrell, L. Fanshier and J. M. Bishop. *J Virol* 6(5):589-598, 1970.

A DNA polymerase associated with Rous sarcoma virus and avian myeloblastosis virus is identified in preparations of the viruses purified through treatment with a nonionic detergent. DNA polymerase activity was dependent upon concentration of detergent as a function of protein concentration of the virus suspension; catalysis of the synthesis of DNA persisted for at least 6 hr at an optimum temperature of 45°C and showed an 8- to 10-fold reduction of activity when pretreated with ribonuclease, a 2- to 3-fold inhibition in the presence of actinomycin D and only slight inhibition with Rifampin. Sedimentation analysis of the early and late products showed a DNA which cosedimented with 70 S viral RNA at neutral pH (30 min) and a mixture of DNA-RNA hybrids and double-stranded DNA (4 hr); at 8 hr, the major product was double-stranded DNA.

1082 THE GROWTH CAPACITY OF NORMAL AND ROUS-VIRUS-TRANSFORMED CHICKEN FIBROBLASTS IN VITRO. (E.) Ponten, J. (Wallenberg Lab., Uppsala, Sweden). *Int J Cancer* 6(3):323-332, 1970.

The proliferation dynamics of chicken embryo cell cultures transformed by Rous sarcoma virus, Schmidt-Ruppin strain (RSV-SR), was compared with that of normal cells. RSV-SR-transformed cells had a decreased average population doubling time (15 hr vs 21 hr for normal cells), and increased maximal terminal cell density (70×10^4 cells/cm² vs 35×10^4 for normal cells) and a shorter life span (10-15 passages compared to 20-27 passages in normal cells). The cumulative cell number of the transformed cells (10^9) was considerably lower than that of untransformed cells (10^{12}), and no established cell lines were developed. RSV-SR-transformed cells from one sex cocultivated with normal cells of the opposite sex resulted in a rapid transformation of the normal cells with the proportion of dividing cells from the originally transformed cells decreasing as the newly transformed cells became dominant. Apparently avian Rous sarcoma proliferates only if normal cells are constantly transformed and added to the pool of transformed or neoplastic cells.

- 1083 STUDIES ON THE LOSS OF GROWTH INHIBITION IN CELLS INFECTED WITH ROUS SARCOMA VIRUS. (E.) Weiss, R. (Dept. Anat. Embryol., U. Coll., London, England). *Int J Cancer* 6(3):333-345, 1970.

The loss of growth inhibition (density-dependent and anchorage-dependent growth) was studied in chick embryo cells infected with Rous sarcoma virus (RSV). Transformed cells and newly infected cells were capable of proliferating in soft gel suspension and among densely populated normal cells. Plating freshly infected cells on crowded mouse embryo cells or 3T3 cells inhibited cell transformation and viral replication, but the majority of infected cells lost their sensitivity to inhibition 6 hr after infection, and all cells were released from inhibition after 12 hr. The quantity or envelope properties of virus released from the cell surface did not influence the changes in proliferative behavior of transformed cells, and preinfection with a Rous-associated virus (RAV) did not alter the density-dependent cell transformation by RSV. Freshly infected cells maintained in the inhibited state for 6 days were capable of transforming when replated to sparse conditions. Cell transformation was dependent on cell proliferation but RSV infection could not initiate the cell division cycle in crowded monolayers.

- 1084 CHROMOSOMAL ANALYSIS OF PRIMARY AND METASTATIC ROUS SARCOMAS IN THE RAT. (E.) Mitelman, F. (Inst. Path. U. Lund, Sweden) and J. Mark. *Hereditas* 65(2):227-236, 1970.

The chromosomes of 13 primary and 4 metastatic Rous Sarcomas in the rat were studied in sections taken directly from the tumors. The stemline number was 42 in 11 of the primary tumors and in 3 of the metastatic tumor cases, but the spread of the overall chromosomes showed a positive skewness. Polyploid cells were uncommon (approximately 1%), and hyperploidy was the most common heteroploid pathway (24% in the primary tumors and 38% in the secondary tumors) while pseudoploidy was the second common pathway (15% in the primary and 50% in the metastatic tumors). Trends towards a nonrandom chromosomal engagement were observed.

- 1085 PROTEINS OF AVIAN TUMOR VIRUSES WITH DIFFERENT COAT ANTIGENS. (E.) Robinson, W. S. (Stanford U. Sch. Med., Calif.), P. Hung, H. L. Robinson and D. D. Ralph. *J Virol* 6(5):695-698, 1970.

The protein components of 2 avian tumor viruses with distinct type-specific envelope antigens were examined by gel electrophoresis. The viruses which were studied, Rous-associated virus type 1 (RAV-1) and Rous sarcoma virus type $\beta(0)$ [RSV $\beta(0)$], had identical isoelectric points, as demonstrated by isoelectric focusing. Coelectrophoresis of ^{14}C -amino acid-RSV $\beta(0)$ and ^3H -amino acid RAV-1 in a polyacrylamide gel containing sodium dodecyl sulfate permitted the identification of 8 labeled protein components in the viruses, numbered P1-P8. P1,

a slowly-moving protein, was the major protein in RSV $\beta(0)$, while P2 was the major protein in RAV-1. The findings, which indicate that these 2 viruses of different type-specific surface antigens have glycoprotein components with differing mobilities in sodium dodecyl sulfate gel electrophoresis, suggest that the glycoproteins are related to the type-specific antigen.

- 1086 RECOVERY OF A NEW VIRUS FROM APPARENTLY NORMAL CHICK CELLS BY INFECTION WITH AVIAN TUMOR VIRUSES. (E.) Hanafusa, T. (Publ. Hlth. Res. Inst. City New York, N.Y.), H. Hanafusa and T. Miyamoto. *Proc Nat Acad Sci* 67(4):1797-1803, 1970.

A new virus was recovered from chick embryo cells containing a genetic factor "chick cell-associated helper factor" (chf). Although the chf could not mature into a complete virus by itself, it became transmissible after infection of C/O type chick embryo cells by avian leukosis virus or Rous sarcoma virus. The newly isolated virus was named RAV-60; it did not require the presence of another virus for its replication. RAV-60 grew in susceptible chick and quail cells; infected cells produced virus at a constant rate with minimal cytopathic effects. The host range of RAV-60 was the same as those of Rous sarcoma virus (RAV-60) and Rous sarcoma virus type $\beta(0)$; Japanese quail cells and Rous sarcoma virus type $\beta(0)$ -susceptible chick embryo cells were susceptible to the virus, and Rous sarcoma virus type $\beta(0)$ -resistant chick embryo cells were resistant to it. RAV-60 was antigenically identical to Rous sarcoma virus type $\beta(0)$ in the specificity and rate of inactivation by anti-Rous sarcoma virus type $\beta(0)$ antiserum. Rous sarcoma virus-RAV-60 had the type $\beta(0)$ specificity as Rous sarcoma virus type $\beta(0)$ in its sensitivity to interference induced by avian leukosis viruses. RAV-60 was structurally similar to Rous sarcoma virus type $\beta(0)$.

- 1087 ISOLATION OF A VARIANT STRAIN OF ROUS SARCOMA VIRUS ONCOGENIC FOR DUCKS AND MAMMALS. (E.) Kuwata, T. (Sch. Med. Chiba U., Japan) and H. Kawakami. *Arch Ges Virusforsch* 32(1):1-12, 1970.

The isolation of a strain of Rous sarcoma virus which proved to be oncogenic for ducks, mice and hamsters was described. The variant strain was developed from the Bryan standard strain (BS-RSV) which is not oncogenic for ducks or newborn mice. Cell suspensions of BS-RSV-induced chicken tumor were injected into ducklings which had been treated with cortisone; this method induced tumors in 4 ducklings, 3 of which regressed, but 1 grew to a large size (5.4 x 2.8 cm). Cells from this tumor were passaged further in ducks; metastases developed in the lung, spleen, liver and heart further confirming the oncogenicity of the BS-RSV variant (BK-RVS) for ducks; crude extracts were passaged for 30 generations without cortisone-treatment and continued to induce tumors in ducks. The oncogenic variant was passaged in ducks and injected into CFW mice, where it produced 1 tumor in 14 injected mice. In other passages in mice, BK-RSV induced tumors in 1/6 CFW mice and 2/8 AKR mice.

in experiments with hamsters, BK-RSV produced tumors in 2 of 6 injected animals. Neither mouse nor hamster tumors produced infectious RSV. However, sarcomas yielding infectious RSV were produced in the lungs of chickens injected with hamster tumor cells.

088 THE LOW MOLECULAR WEIGHT RNAs OF ROUS SARCOMA VIRUS: II. THE 7 S RNA. (E.) Bishop, T. M. (U. California Sch. Med., San Francisco), W. E. Levinson, D. Sullivan, L. Fanshier, N. Quintrell and Jackson. *Virology* 42(4):927-937, 1970.

The structure and chemistry of the 7S RNA of the Bryan and Schmidt-Ruppin strains of Rous sarcoma virus were investigated. The 7S RNA, which was purified by chromatography on columns of methylated albumin kieselguhr, appeared to be a single-stranded molecule with a molecular wt of 80,000. The nucleotide composition of the 7S RNA (which comprised 3-5% of the total viral RNA) was different in the 2 strains of virus, and was different from any known cellular RNA; an exceptionally high guanine plus cytosine content was found. This RNA was not appreciably methylated, suggesting that it is not a form of transfer RNA. Neither the 7S RNA nor the 4S transfer RNA were complementary to the Rous sarcoma virus genome, and no corresponding form of RNA could be identified in either normal or infected cells.

089 CHANGES IN DEOXYRIBONUCLEIC ACID SYNTHESIS REGULATION IN CHINESE HAMSTER CELLS INFECTED WITH SIMIAN VIRUS 40. (E.) Lehman, J. M. (U. Colorado Med. Sch., Denver) and V. Defendi. *J. Virol.* 6(6):738-749, 1970.

The patterns of cellular DNA synthesis in Chinese hamster cells after SV40 infection were studied to determine the relevance of cellular DNA induction to the phenomenon of cell transformation. No cell lysis was observed after SV40 infection but at a multiplicity of infection (MOI) of 50, 80-95% of the cells contained the virus-specific intranuclear antigen within 72 hr. In ³H-thymidine studies (0.2 µCi/ml) the infected cells had 85-90% labeled nuclei after 22-24 hr compared to the 50% of controls indicating that the SV40 infection stimulated DNA synthesis (only 2% of the newly synthesized DNA was viral DNA). Transformed cells were apparent in the infected cultures several weeks after infection and produced tumors (fibrosarcomas) at the injection site when injected into irradiated hamsters. The striking difference between infected and control cultures was a rapid increase in cells with 8n DNA content (from a steady 2% in controls to 4% at 6 hr, 18% at 36 hr, and 30-50% at 4 weeks in infected cells). The polyploid cells apparently resulted from an induction of 2 successive rounds of DNA synthesis in a G₁, S, or G₂ cell without an intervening mitosis.

090 SV40 THERMOSENSITIVE MUTANT: SYNTHESIS OF VIRAL DNA AND VIRUS-INDUCED PROTEINS AT NONPERMISSIVE TEMPERATURE. (E.) Takemoto, K. K. (Natl. Inst. Allerg. Infect. Dis., Natl. Inst. Hlth., Bethesda, Md.) and M. A. Martin. *Virology* 42(4):938-945, 1970.

The synthesis of viral DNA and virus-induced proteins at a nonpermissive temperature (40°C) was studied in the SV40 thermosensitive mutant (SV-L) grown in primary African green monkey kidney cells. Complement fixation and an indirect fluorescent antibody technique demonstrated that viral antigen and T-antigen were produced by infected cell extracts at similar titers at 37°C (128 and 64, resp.) and at 40°C (64 and 64, resp.), but the infectivity was higher at the lower temperature (1.5×10^9 compared to 5×10^5) plaque-forming units/ml. The physical properties (configuration, molecular size, polynucleotide sequence, and infectivity) of the viral DNA made at the nonpermissive and permissive temperatures were similar, although electron microscopy revealed fewer intranuclear virus particles in the cells infected at the higher temperature. SV-L virions formed at the permissive temperature were extremely thermolabile (0.001% survival after 60 min at 50°C) compared to the 100% survival of SV-S virions, the small-plaque mutant, indicating defects in the structural protein of SV-L.

1091 ALTERATION IN GANGLIOSIDE PATTERN AND SYNTHESIS IN SV40- AND POLYOMA VIRUS-TRANSFORMED MOUSE CELL LINES. (E.) Brady, R. O. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and P. T. Mora. *Biochem Biophys Acta* 218(2):308-319, 1970.

Changes in the ganglioside pattern of mouse cells caused by transformation by tumorigenic DNA viruses, including polyoma virus and SV40, were investigated. Ganglioside patterns of virally transformed cells were drastically altered compared to parent cell lines and spontaneously transformed cell lines. A reduction in the amount of the highest ganglioside homolog, *N*-acetylneuraminylgalactosyl-*N*-acetylgalactosaminyl-(*N*-acetylneuraminyl)-galactosylglucosylceramide (G_{D1a}), and an increase in *N*-acetylneuraminylgalactosylglucosylceramide (G_{Ma}), which becomes the principal ganglioside, were found. When strain AL/N mouse cells were transformed by DNA viruses, G_{D1a} and galactosyl-*N*-acetylgalactosaminyl-(*N*-acetylneuraminyl)-galactosylglucosylceramide (G_{M1}) were decreased from 1.8 and 1.5 nmoles/mg protein in normal cells to 0.14 and 0.08 nmoles/mg in polyoma virus-transformed cells, resp. When Swiss mouse cells were transformed by viruses, G_{D1a} and G_{M1} decreased, and hematoside (*N*-acetylneuraminylgalactosylglucosylceramide) (G_{M3}) became the principal ganglioside homolog, a result which was far more pronounced in cells cultured in Dulbecco-Vought medium than in cells cultured in Eagle's medium. Similar results were obtained by transforming BALB/c cells with either SV40 or polyoma virus. The dynamics of ganglioside reduction and increase in virally transformed cells were confirmed by incorporation studies with radioactive precursors. A common virus-regulated biochemical function appears to be present in SV40 and polyoma virus-transformed mouse cells, which is expressed in these changes in the membrane glycolipids of transformed cells.

1092 SUPERINFECTION OF SIMIAN VIRUS 40 TRANSFORMED PERMISSIVE CELLS WITH SIMIAN VIRUS

40. (E.) Barbanti-Brodano, G. (Inst. Microbiol., U. Bologna, Italy), P. Swetly and H. Koprowski. *J Virol* 6(5):644-651, 1970.

The capacity of a clone of African green monkey kidney cells previously transformed with SV40 to adsorb superinfectious doses of SV40 was investigated. Normally, SV40 permissive transformed cells adsorbed only negligible amounts of virus. When the transformed cells were incubated for 90 min with a homogenate of mouse embryo fibroblasts infected with polyoma virus, they adsorbed 20 times more virus than did untreated cells. Within 15 min after exposure to ^3H -labeled SV40 superinfection, treated cells had taken up 2.2% of the labeled virus; by 90 min postinfection, 4.5% of the virus had been adsorbed; thereafter, adsorption fell off slightly. Pretreatment of SV40-transformed cells with histones resulted in a 17-fold higher uptake of SV40 than was observed in untreated cells, and treatment with diethylaminoethyl dextran and a homogenate of noninfected mouse embryo fibroblast also enhanced the adsorption of SV40. Treatment of SV40-transformed cells with purified polyoma virus, receptor-destroying enzyme, neuraminidase, trypsin, heparin and dextran sulfate did not affect adsorption. Under conditions of enhanced viral adsorption, SV40 particles penetrated the nuclei of cells. The number of cells producing viral protein in superinfected transformed cultures was 15-fold greater than in untreated transformed cultures; the virus yield of SV40 superinfected transformed cells was 7 times less than the virus yield of African green monkey kidney cells 3 days after infection.

1093 SV40-TUMORIGENESIS IN MOUSE. (E.) Wesslen, T. (Inst. Med. Microbiol., U. Uppsala, Sweden). *Acta Path Microbiol Scand* 78(4):479-487, 1970.

The oncogenicity of SV40-transformed cells was investigated in mice after passage *in vitro* and *in vivo*. Virus-transformed cell lines were derived from kidneys and embryos of mice infected with SV40 at multiplicities of about 100 and tested for oncogenicity by injection into syngeneic mice (50×10^6 cells). Some mice receiving infected cells had been irradiated previously with 400 rads of whole-body X-irradiation. Infected kidney cells cultured for 1-6 months which were injected into mice produced small regressive tumors in a few cases, but otherwise were ineffective. When embryo cells infected with SV40 were injected into mice after 8 and 9 months in culture, walnut-sized regressive tumors appeared in irradiated mice, as well as a progressively growing tumor in 1 irradiated mouse. The mouse embryo cell line proved to be more actively oncogenic than the kidney cell line, the latter never producing tumors except for regressive ones in irradiated animals. After 4 *in vivo* passages, the SV40-containing tumor cells developed by an irradiated mouse were able to produce tumors in both irradiated and unirradiated mice. After multiple passages *in vivo*, the character of the tumor changed to an infiltratingly growing sarcoma metastasizing to regional lymph nodes. In repeated oncogenicity tests of *in vivo*-passaged

tumor cells, it was found that passaged cells produce tumors only in irradiated mice before they had undergone at least 2 passages, and thereafter produced tumors in all mice. At the third passage level 10^7 cells were required to produce tumors, while at the 22nd passage level, 10^4 cells produced tumors in 1 of 3 injected mice. The *in vitro* mouse embryo cells were cloned, as were cells from the 22nd *in vivo* passage; none of the cloned cells from the *in vitro* cells produced tumors, while clones from the *in vivo* passaged cells (10^3) produced tumors in most of the tests. All the cell lines contained SV40 until the 3rd wk after virus inoculation, after which SV40 could not be recovered from any line. Most tumor material did not contain SV40 specific complement-fixing antigen; the antigen titers of tumor cells which varied from 1:8-1:32 were not correlated to tumorigenicity. Animals carrying SV40 induced tumors had high titers of immunofluorescent antibodies for long periods of time to the SV40 neoantigen in their sera.

1094 THE SV PSEUDOVIRUS: ITS POTENTIAL FOR GENERAL TRANSDUCTION IN ANIMAL CELLS. (E.) Grady, L. (New York St. Dept. Hlth., Albany), D. Axelrod and D. Trilling. *Proc Nat Acad Sci* 67(4):1886-1893, 1970.

This report presents evidence that the SV40 pseudovirus is a potential general transducing virus based on measurements of reassociation rates and the finding that Vero cell DNA incorporated into pseudoviruses can be introduced into mouse embryo cells and penetrate the cell's nucleus without loss of physical integrity. Data demonstrate that DNA from pseudoviruses more closely resembles that of Vero cells than it does the DNA of mature SV40. Rates of reassociation of fast sequences of Vero cells and from pseudoviruses are similar with less than 1% nonspecific binding being observed in the initial sample; similarity in temperature stability of reassociated unique sequences indicated the precision of base pairing in Vero-pseudovirus hybrids to be similar to that of the reassociated, unique sequences of Vero DNA. Pseudoviruses entered the mouse embryo cell and in both stationary and dividing cultures approximately 10% penetrated the nuclei. Lysis of the nuclei and sedimentation yielded ^{32}P -DNA profiles identical to those of pseudovirus DNA even to the ratio of the amounts of 5S and 18S DNA. The SV40 pseudovirus and general transducing bacteriophage appear to be analogous in several respects.

1095 TRANSFORMATION OF HUMAN CELLS WITH DIFFERENT FORMS OF SV40 DNA. (E.) Aaronson, S. A. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.) and M. A. Martin. *Virology* 42(4):848-856, 1970.

The transformation of human fibroblast cells and the induction of T-antigen by the supercoiled DNAs (form I) of the small (SV-S) and large (SV-L) plaque variants of the tumor virus SV40 and by a mixture of open circular (form II) and linear forms of SV-S DNA were investigated. The whole SV-S

rus was 100 times more efficient than the SV-L virus in inducing T-antigen, but DNA I from both viruses exhibited similar induction levels (0.5-3% plateau levels with 0.4 μ g DNA I). The number of transformed colonies obtained with 0.4 μ g of DNA I is similar for SV-S and SV-L (0.06 and 0.1 colony/ 10^6 cells), and the cellular morphology of the colonies transformed with DNA closely resembled that observed with whole virus. Mixtures of the open circular and linear forms of SV-S DNA (0.05 μ g) were capable of inducing T-antigen (0.2%), transforming cells (20 transformants/ 10^6 cells), and yielded infectious progeny (1.1×10^5 plaque-forming units/ μ g DNA), but fragmented linear SV-S DNA (mechanically sheared in a French-type pressure cell) ranging in size from $3.0-8.6 \times 10^5$ daltons did not induce T-antigen or yield infectious virus.

96 TRANSFORMATION OF MOUSE MACROPHAGES BY SIMIAN VIRUS 40. (E.) Stone, L. B. Natl. Inst. Allergy, Infect. Dis., Natl. Inst. Health, Bethesda, Md.) and K. K. Takemoto. *J Virol* 5:621-627, 1970.

The ability of SV40 to transform mouse peritoneal macrophages was investigated. Macrophage cultures were infected by SV40 at a multiplicity of 10, and DNA synthesis and tumor antigen production were assayed to determine whether the normally non-dividing macrophage cells were proliferating. Tumor antigen was first seen at 24 hr after SV40 infection; by 72 hr the percentage of tumor-antigen positive cells had risen from 1% at 24 hr to 75%, and by 144 hr postinfection, 100% of the cells had tumor antigen. DNA synthesis was first observed 24 hr after infection, at which time the uptake of 3 H-thymidine into trichloroacetic acid-insoluble DNA at 1 hr was $10^{2.5}$ cpm. Seventy-two hr after infection, values for 3 H-thymidine uptake were $10^{3.75}$ cpm; after this point, DNA synthesis declined precipitously, thymidine uptake values returning to 10^2 cpm by 120-144 hr postinfection. During the tumor-antigen-producing period, it was possible to rescue SV40 from nondividing unaltered macrophages. About 66 days postinfection proliferating transformants appeared in the infected cultures. When these cells were cultured, they were found to be tumor antigen-positive and virus-negative. However, because of their morphological similarity to macrophages and their exhibition of phagocytosis, acid phosphatase, β_1 synthesis, and aminoacridine incorporation, these cells were thought to be transformed macrophages.

97 TRANSFORMATION OF RAT LYMPH NODE CELLS BY SIMIAN VIRUS 40: ATTEMPT TO "FIX" SPECIALIZED FUNCTION. (E.) Collins, J. J. (Massachusetts Gen. Hosp., Boston), K. J. Bloch and P. H. Black. *Nat Cancer Inst* 45(6):1097-1104, 1970.

In vitro production of a nonspecific antibody in response to oncogenic simian virus 40 (SV40) was attempted with suspension cultures of cells from pooled lymph nodes from rats hyperimmunized with phytohemagglutinin (PHA) and dinitrophenyl bovine serum albumin (DNP-BSA). At 40 hr after infection,

samples of cells revealed no SV40 T antigen either through inability of cells to support synthesis or undetectability by the indirect fluorescent antibody technique. At 34 days, few cultures showed lymphoblast transformation characterized by numerous prominent nucleoli and giant cells. Established cell lines upon fluorescent antibody staining revealed granular nuclear fluorescence characteristic of SV40 T antigen. Transformed cells grown in the presence of 14 C-leucine failed to incorporate labeled amino acid into the immunoglobulin molecules. Neither the transformed lines growing on glass nor untransformed lymphocytes in suspension at 5-7 wk after seeding appeared to synthesize rat immunoglobulin. Either infection of antibody producing cells did not occur or transformation was accompanied by a loss of specific function.

1098 RELATIONSHIP BETWEEN MOLECULAR LENGTH AND BIOLOGICAL ACTIVITY OF SV40 DNA. (E.) Yamamoto, S. (Okayama U. Med. Sch., Japan), S. Omura and T. Oda. *Acta Med Okayama* 24(3):273-285, 1970.

A correlation between the length of the DNA molecule in SV40 and the infectivity of the virus was observed. DNA was extracted from three separate groups of SV40: high-titered original virus, undiluted passaged original virus, and diluted passaged virus of the second group. Mean length of the DNA molecules in each group was, resp., 1.50 μ , 1.40 μ , and 1.47 μ . Undiluted passage of virus caused shortening of DNA and defective virus of low infectivity was produced; however, if the defective virus group received dilute passage again, infectivity was restored. Small circular DNA molecules shorter than 1 μ were observed in virions prepared from undiluted passages. Dimers and replicating forms of defective SV40 DNA were observed both in purified virion and in the nuclei of SV40 infected African green monkey kidney cells.

1099 EFFECT OF H-1 VIRUS INFECTION ON RNA SYNTHESIS IN NB CELLS. (E.) Fong, C. K. Y. (Putnam Mem. Hosp. Inst. Med. Res., Bennington, Vermont), H. W. Toolan and M. S. Hopkins. *Proc Soc Exp Biol Med* 135(3):585-588, 1970.

The effect of infection with H-1 strain virus on RNA synthesis in a cell line originally derived from SV40-transformed newborn human kidney cells (NB) was investigated. Monolayer cultures of NB cells were infected with H-1 at an input multiplicity of about 10-15, and RNA synthesis was assayed using cells labeled with 3 H-uridine. Cytopathic changes in the infected cells were first detected 24 hr after infection; at later stages, nuclear vacuolation, chromatin depletion, and disappearance of nucleoli were observed. The rate of RNA synthesis in infected cells rose sharply between 9-15 hr postinfection, and declined between 15-20 hr postinfection from 3.8 to 1.8 cpm of 3 H-uridine incorporated/ 10^5 cells/hr. From 15 hr postinfection, the rate of RNA synthesis in infected NB cells remained lower than that of uninfected cells (1.7 and 2.8 cpm 3 H-uridine/ 10^5 cells/hr at 20 hr postinfection; at 70 hr postinfection the rates were

0.3 and 1.7 cpm, resp.). The increase in uptake of uridine into RNA in H-1 virus-infected cells after infection was also observed in autoradiographic studies. After infection, the percentage of cells labeled with ³H-uridine in infected cultures declined from 100% at 8 hr to 23% at 48 hr. Uninfected cells continued to be labeled at about the 100% level till 48 hr postinfection. Gel electrophoresis showed that the 28S ribosomal RNA was selectively inhibited by viral infection, while stimulation was observed in the low molecular wt 4S RNA.

- 1100 VARIATION IN RESPONSE OF SYRIAN HAMSTER LUNG CELLS TO COMPLETE OR DEFECTIVE SV40 (PARA). (E.) Nachtigal, M. (Baylor Coll. Med., Houston, Texas) and J. S. Butel. *Proc Soc Exp Biol Med* 135 (3):727-731, 1970.

The cytopathic and antigenic responses of hamster lung fibroblasts to infection by intact or defective SV40 was investigated. Hamster lung cells in culture were infected with SV40 or with a defective strain of SV40 (PARA) in amounts of 20 plaque forming units (PFU)/cell of SV40 and 0.06 PFU/cell of PARA. No cytopathic effects were in evidence following infection of hamster fibroblasts with SV40; however, all cultures exposed to PARA exhibited transitory cytopathic effects. PARA- and SV40-transformed hamster fibroblast lines were tested by immunofluorescence for the presence of SV40 tumor and specific antigens, and for adenovirus tumor antigen. Six cell lines derived from cultures transformed by different clonal lines of PARA all contained SV40 tumor antigen. Cell lines transformed by SV40 exhibited no SV40 tumor antigen. All PARA-transformed cell lines contained SV40 specific antigen at the cell membrane, but specific antigen was not found in cells transformed by SV40.

- 1101 SIALIC ACID TRANSFERASES AND SIALIC ACID LEVELS IN NORMAL AND TRANSFORMED CELLS. (E.) Grimes, W.J. (Massachusetts Inst. Tech., Cambridge). *Biochemistry* 9(26):5083-5092, 1970.

The ability of particulate enzyme preparations from normal and SV40-transformed 3T3 Swiss and BALB/c mice cells to catalyze sialic acid transfer to glycoproteins was determined. Preparations from transformed 3T3 cells had only 55-60% of the sialyl transferase activity as normal cells, while preparations from spontaneously transformed cells had intermediate activity; transformed BALB/c cells had 31% as much sialyl transferase activity as normal cells. Incorporation of radioactivity into glycoproteins was stimulated 10% by 0.1% Triton-X. The optimal hydrogen ion concentration for the transferase was pH 6.5. The total sialic acid concentration/mg protein of the particulate cell fractions (which contained over 80% of the total cellular sialic acid) in transformed cells was 35% and 60% of that found in normal BALB/c and 3T3 cells, resp.

- 1102 CELL DENSITY-DEPENDENT CHANGES OF GLYCOLIPID CONCENTRATIONS IN FIBROBLASTS, AND LOSS OF THIS RESPONSE IN VIRUS-TRANSFORMED CELLS. (E.) Hakomori, S. (U. Washington Sch. Hlth. Commun. Med., Seattle). *Proc Nat Acad Sci* 67(4):1741-1747, 1970.

In the present investigation glycolipids of normal hamster kidney and human fibroblastic cultured cells at different stages of growth and with varying degrees of contact inhibition were analyzed and compared with the glycolipids of virally transformed cells. The concentration of galactosylgalactosylglucosyl-, N-acetylneuraminosylgalactosylglucosyl-, and N-acetylneuraminosyl-(N-acetylneuraminosyl)galactosylglucosyl-ceramide increased at high cell densities with decrease in concentration on successive passages or after malignant transformation of the cells. Glycolipids of human diploid fibroblasts showed a 1- to 2-fold increase with cell confluence and disappeared or were greatly reduced in concentration after transformation. Regulation of synthesis and degradation of carbohydrate chains showing density-dependent response, possibly through a contact-sensitive enzyme system, may be of crucial importance in understanding various phases of cell-sociologic phenomena, such as malignancy.

- 1103 SIMIAN VIRUS 40 DEOXYRIBONUCLEIC ACID TRANSCRIPTION *IN VITRO*: BINDING AND TRANSCRIPTION PATTERNS WITH A MAMMALIAN RIBONUCLEIC ACID POLYMERASE. (E.) Herzberg, M. (Weizmann Inst. Sci., Rehovot, Israel) and E. Winocour. *J Virol* 6(5):667-676, 1970.

The *in vitro* binding pattern of mammalian RNA polymerase to simian virus 40 (SV40) DNA was studied by electron microscopy and velocity sedimentation techniques. An estimated 2.0 µg of RNA polymerase was required to saturate the binding sites in 0.1 µg of SV40 DNA. The majority of supercoiled SV40 DNA molecules revealed only a single binding site for mammalian RNA polymerase and a single chain of nascent RNA attached to the SV40 DNA template during transcription. The finding of a single binding site for RNA polymerase indicates that only part of the viral genome is transcribed *in vitro*.

- 1104 ELECTRON-MICROSCOPIC OBSERVATIONS OF POLYOMA VIRUS-TRANSFORMED MOUSE CELLS TREATED WITH SPECIFIC IMMUNE SERUM. (E.) Negroni, G. (Imperial Cancer Res. Fund., London, England) and R. Tilly. *J Cell Sci* 7(3):711-718, 1970.

Morphological changes in mouse cells transformed by polyoma virus and treated with virus-specific immune serum were observed by electron microscopy. Transformed nonmalignant cells were treated either with specific antiserum induced in mice by 6 i.p. inoculations of 10⁶ nonmalignant cells or with serum from untreated mice. In all experiments cells were also treated with complement. No morphological changes occurred in the cells treated with control serum and complement, while in cells treated with immune serum and complement, complete disruption of cells was observed. In another experiment in which mixtures of immune serum and complement were incubated with nonmalignant transformed cells for differing lengths of time, there were no morphological changes in nonmalignant transformed cells treated with control serum and complement, in nonmalignant transformed cells treated with immune serum only, and in normal mouse embryo cells treated with con-

rol (or immune) serum and complement. Changes in on-malignant transformed cells treated with immune serum and complement included discontinuity of cell membranes; the numbers of cells showing interruption of cell membranes increased with the duration of contact with complement and immune serum. Damaged cells showed a peripheral emptiness due to loss of organelles through the membrane lesions.

105 INHIBITION BY TOYOCAMYCIN OF RNA SYNTHESIS IN MAMMALIAN CELLS AND IN NORMAL AND AVIAN TUMOR VIRUS-INFECTED CHICK EMBRYO CELLS. (E.) Verak, L. (Duke U. Med. Ctr., Durham, N.C.), R. A. Conar, A. J. Langlois and J. W. Beard. *Biochem Biophys Acta* 224(2):441-450, 1970.

The effect of toyocamycin on RNA synthesis in mammalian cells and in normal and virus-infected chick embryo cells was investigated by density gradient centrifugation. Chick embryo cells and L cells were incubated with toyocamycin (0.1-2.0 µg/ml) for 20 min and labeled with ³H-uridine (chick embryo cells) or ¹⁴C-uridine (L cells). Without toyocamycin incorporation of radioactive uridine approached equilibrium with some radioactivity in the 45S region. Toyocamycin suppressed uridine incorporation into the 18S and 28S RNA in both cell species; in L cell RNA, but not in chick embryo RNA, there was a slight increase in radioactivity in the 45S region and a shift of 1 fraction of the radioactivity peak from the 28S to the 32S position. Increasing the dose of toyocamycin towards 2.0 µg/ml further suppressed L cell uridine uptake in the 45S region, and continued to suppress ribosomal RNA synthesis in chick embryo cells generally. The differences in the response of the 2 cell species to toyocamycin may reflect different enzyme sensitivities; the inhibitory effect of toyocamycin in chick cells may have been on both synthesis and conversion of the 45S precursor RNA. The nucleolar RNA formed in chick cells infected with MC29 virus was mainly ribosomal RNA precursor with no clear evidence of virus-specific RNA; this RNA was toyocamycin-resistant. Toyocamycin treatment caused nucleolar fragmentation and wide dispersion of nucleolar components in chick embryo cells, virus-infected chick cells and myeloblasts of BAI strain A virus leukemia.

106 FORMATION OF CELLULAR DEOXYRIBONUCLEIC ACID DURING PRODUCTIVE POLYOMA VIRUS INFECTION. (E.) Cheevers, W. P. (Cancer Res. Lab., J. Western Ontario, London, Canada), P. E. Branton and R. Sheinin. *J Virol* 6(5):573-582, 1970.

The formation of cellular DNA during productive polyoma infection at low input multiplicities (1-10 plaque-forming units/cell) in primary and secondary cultures of mouse embryo cells was studied using neutral and alkaline sucrose gradients. An increased rate of cellular DNA synthesis followed with ³H-thymidine (25,489 cpm compared to a control 21,609 cpm) was observed 15-18 hr after infection, but viral DNA synthesis was not detected until 3 hr later when 3% (898 cpm) of the total DNA synthesized was viral. After 27-30 hr, 86% of the DNA

synthesized was cellular and 14% was viral. DNA synthesized in polyoma-infected cells up to 18 hr after infection was of the same molecular size as the normal pre-infection DNA, but after 18 hr, the DNA consisted of 3 separate components: one component cosedimented with the normal cell DNA, another component sedimented as form I polyoma DNA, and the third component sedimented as a heterogeneous component consisting of discontinuous newly synthesized strands of cell DNA and arising by direct synthesis (not by degradation of the high molecular weight normal cell DNA) only after the initiation of viral DNA synthesis. The heterogeneously sedimenting component was then converted to normal cell DNA without prior degradation to acid-soluble components. The pattern of DNA synthesis is apparently altered late in the infection by a process associated with the replication of viral DNA.

1107 STUDIES ON THE IMMUNOCHEMICAL BASIS FOR ANTIGENIC VARIATION AMONG POLYOMA VIRUS STRAINS. (E.) Hare, J. D. (U. Rochester Sch. Med., N.Y.) and J. C. Chan. *J Nat Cancer Inst* 45(6):1179-1188, 1970.

Two serologically distinct plaque-sized variants of polyoma virus were examined by immunochemical analysis in order to determine the mechanism of their differing serological behavior. The cross-reactions of 2 polyoma virus strains, 210 and 3049, were determined by semiquantitative immunodiffusion with homologous and heterologous antisera. The 3049 preparation was 8 times more concentrated than the 210 preparation, and the titer of each virus strain was independent of the antiserum used to measure the antigen content. The antibody content of the anti-3049 antiserum was 4 times higher with homologous antigen than with heterologous antigen; with the anti-210 serum, the homologous antigen titer was about 8 times greater than the heterologous titer. In semiquantitative cross-absorption studies, dilutions of antisera were reacted with dilutions of homologous and heterologous antigen preparations, after which the ability of these absorbed antisera to form precipitin lines with the 2 antigens was tested in an agar diffusion system. When anti-3049 serum was absorbed with either 3049 or 210 preparations, antibody activity to both antigens was removed. Less 210 antigen than 3049 antigen was required to remove both anti-210 and anti-3049 activity. When the anti-210 serum was adsorbed with either virus, anti-3049 activity was removed by roughly equivalent amounts of either 3049 or 210 antigen. This finding appeared to suggest that anti-210 serum contained an antibody directed against an antigenic determinant represented on the 210 virus which was either hidden, absent, or significantly reduced in quantity in the 3049 virus population. The precipitin patterns which developed when anti-210 and anti-3049 sera reacted with 210 and 3049 antigen preparations indicated that the 3049 virus preparation contained a major antigenic determinant, "L", which was also present in the 210 virus. The 210 virus contained a major antigenic determinant, "S", which was un-

detectable in 3049 virus. However, hyperimmune anti-3049 rabbit serum did contain antibody to S, suggesting that this antigen is present in 3049 virus preparations, but in reduced quantities or sterically hidden. The S antigen did not cross-react with a small plaque variant of Toronto polyoma virus.

- 1108 DENSITY-DEPENDENT INHIBITION OF PROTEIN SYNTHESIS IN NORMAL AND VIRUS-TRANSFORMED CELLS. (E.) Waller, J. M. (Dept. Path., U. Chicago, Ill.) and W. H. Kirsten. *Virchow Arch Zellpath* 6(3):183-197, 1970.

Comparison of density-dependent inhibition between normal mouse cells and two cell lines transformed by polyoma and simian virus 40, and murine sarcoma virus was made by cocultivation, variations in serum concentrations, frequency of medium changes and cell overlays. The rate of protein synthesis increased initially 100-150% per day during logarithmic growth, reached a maximum, and then fell off to 0-10% at saturation density in the three cell lines with reduction occurring at a significantly lower cell density in the normal line. Growth characteristics of cocultivated cells were those of the transformed cells with protein synthesis decreasing only when cell population reached a relatively high cell density. Protein synthesis in normal cells treated by frequent washing and feeding was inhibited in a pattern characteristic of the virus-transformed cell lines with a 30% increase in final total protein content reached in frequently fed cell cultures when compared with cells fed every two days. When normal mouse cell culture was overlaid by 4.8×10^6 cells, protein synthesis was inhibited 49% by 12 hr after overlay; protein synthesis was inhibited only 20% when 20×10^6 transformed cells were overlaid on a homotypic cell culture. A difference in sensitivity to density inhibition of protein synthesis apparently exists between normal and transformed cells.

- 1109 TEMPERATURE-DEPENDENT PROPERTIES OF CELLS TRANSFORMED BY A THERMOSENSITIVE MUTANT OF POLYOMA VIRUS. (E.) Dulbecco, R. (Salk Inst. Biol. Stud., San Diego, Calif.) and W. Eckhardt. *Proc Nat Acad Sci* 67(4):1775-1781, 1970.

The effects of temperature-sensitive mutants of polyoma virus, ts-3 on the characteristics of BALB-3T3 cells transformed in tissue cultures were studied by the use of labeled thymidine and radioautography. There is some induction of cellular DNA synthesis in ts-3-infected cells at 39°C but the proportion of cells incorporating thymidine at 32°C is greater as is the induction of movement. Whereas topoinhibition is temperature-dependent for the ts-3-transformed cells, neither wound serum requirement nor growth in agar showed temperature-dependence. Possibly, temperature-dependent mechanisms can be controlled by the product of the ts-3 gene.

- 1110 THE EFFECT OF CYCLOHEXIMIDE ON DNA SYNTHESIS IN CELLS PRODUCTIVELY-INFECTED WITH POLYOMA VIRUS. (E.) Branton, P. E. (Ontario Cancer Inst., U. Toronto, Canada), W. P. Cheevers and R. Sheinin. *Virology* 42(4):979-992, 1970.

The pattern of DNA synthesis in mouse embryo cells productively infected with polyoma virus was studied with column chromatography and velocity sedimentation in the presence of cycloheximide (10 µg/ml). Cycloheximide reduced the synthesis of mature viral DNA to 3% of the control values and of cellular DNA to 22% of the control value with none of the aberrant cell DNA normally found late in polyoma infected cultures. The drug reversibly blocked the synthesis of mature 20S polyoma DNA, while viral DNA material sedimented heterogeneously at 16-20S on neutral sucrose gradients. Aberrant cell DNA synthesis may be linked to the ring closure (which is apparently the final step in the maturation process) of the circular DNA of polyoma virus.

- 1111 LACK OF INTERACTION BETWEEN POLYOMA VIRUS CAPSID AND MOUSE CELL DNA *IN VITRO*. (E.) Ho, J. K. (Indiana U. Med. Ctr., Indianapolis), G. Y. Chan and J. C. Chan. *Life Sci* 9(21):1255-1260, 1970.

The degree of interaction between polyoma virus (PV) capsid protein and DNA in mouse embryo fibroblasts was investigated. The empty capsid of PV was incubated with tritiated DNA from mouse embryo fibroblasts for varying periods of time, and the hemagglutinating activity of the PV and the presence of ^3H label in the precipitate of a PV-anti-PV serum reaction were examined. Incubation of PV and mouse embryo fibroblast DNA did not result in any significant reduction of hemagglutination titers of PV; an increase in the amount of DNA added to the reaction also did not reduce the hemagglutination titer. No significant amount of ^3H label was recovered from the reaction mixture containing DNA, PV and anti-PV serum. Apparently, no complex formation between PV capsid and mouse cell DNA occurred *in vitro*.

- 1112 EFFECTS OF ARGININE DEPRIVATION ON POLYOMA VIRUS INFECTION OF MOUSE EMBRYO CULTURES. (E.) Winters, A. L. (Sch. Med. U. Pennsylvania, Philadelphia) and R. A. Consigli. *J Gen Viro* 10(1):53-63, 1970.

The effects of arginine deprivation on polyoma virus activity in infected cultures of mouse embryo cells was investigated. Cultures were grown and maintained in Eagle's medium, from which amino acids were selectively withdrawn in the experiments. Polyoma virus synthesis appeared to depend on the presence of all the amino acids in the medium, but was most dependent on arginine, lysine and valine. Arginine deprivation inhibited viral synthesis to about 95%. Arginine deprivation also extended the eclipse period of the virus from 36-72 hr, and in-

hibited plaque-forming activity and hemagglutinating activity during the eclipse period. Plaque-forming activity was inhibited by as much as 90% by arginine deprivation; at 50 hr after infection, log PFU/ml of hemagglutination units in arginine-depleted cells were recorded as 9, while values for complete medium viruses were 30. Polyoma virus DNA synthesis was decreased by 60% by arginine deprivation; however, arginine deficiency did not effect the number of cells synthesizing antigens. Virus synthesis recovered within 7 hr after the addition of arginine to the depleted medium, suggesting that arginine deprivation may have inhibited a late step in virus synthesis. The encapsidation of viral DNA in arginine-depleted cultures was inhibited by about 10%.

- 1113 POTENTIATION OF VIRAL CARCINOGENESIS BY IMMUNOSUPPRESSION. (E.) Allison, A. C. Clin. Res. Cntr., Northwick Park, Harrow, Middlesex, U.K.). *Brit Med J* 4(5732):419-420, 1970.

The effect of immunosuppression on tumor development in mice infected with polyoma virus was investigated. It was observed that inoculation of newborn mice with virus produced a high incidence of tumors, whereas inoculation of adult mice seldom produced tumors. To test the hypothesis that the low inducibility of tumors in adult mice was a result of increased immunocompetence in adults, mice were thymectomized, infected with polyoma virus, and given weekly injections of antilymphocyte serum. When tumors began to appear, some mice were given adult lymphoid cells to restore immunocompetence, and others were given lymphoid cells already sensitized against the antigens of the polyoma virus-induced tumor. No tumors developed in this last group, while the other experimental group and controls which had been thymectomized and infected but which had not received restorative doses of lymphoid cells developed tumors in nearly 100% of cases. These findings suggested that adult mice were protected because they were able to mount an effective immune response against polyoma virus-induced tumors. In another experiment, adult and newborn mice were inoculated with polyoma virus. Ten days and 6 wk later their lymphoid cells were tested for sensitization to the virus by transferring lymphoid cells from these mice to mice which had been inoculated with polyoma virus. Lymphoid cells from the adult mice prevented tumor development in recipient mice. Lymphoid cells from newborns prevented tumor development when taken 6 wk after inoculation with virus; they did not prevent tumor development when taken 10 days after inoculation. Apparently, cell-mediated immunity develops slowly in newborns, and is therefore unable to check tumor development.

- 1114 GLYCOPROTEIN SYNTHESIS AND DEGRADATION: GLYCOPROTEIN:N-ACETYL GLUCOSAMINE TRANSFERASE, PROTEOLYTIC AND GLYCOSIDASE ACTIVITY IN NORMAL AND POLYOMA VIRUS TRANSFORMED BHK CELLS. (E.) Bosmann, H. B. (U. Rochester Sch. Med. Dent., N. Y.) and G. Z. Pike. *Life Sci* 9(24):1433-1440, 1970.

Glycoprotein synthesis and degradation in virus-transformed hamster kidney cells was investigated. Normal hamster kidney cells and hamster kidney cells transformed by polyoma virus were grown in monolayer cultures for assay of glycoprotein-related enzymes. In normal cells, enzymes could be found in 3 groups: those with no activity or less than 20 nmole/hr/mg protein, those with more than 20 nmole/hr/mg but less than 150 nmole/hr/mg, and those with more than 150 nmole/hr/mg. In normal cells, enzymes in the first group included α -D-glucosidase, β -D-glucosidase and α -L-fucosidase; enzymes in the second group included N-acetyl-D-galactosaminidase and acid phosphatase; enzymes in the third group included α -D-galactosidase and N-acetyl- β -D-glucosaminidase. In each instance except β -D-glucuronidase, the polyoma virus-transformed cells had higher levels of enzyme activity than the normal cells. α - and β -D-Glucosidase and β -D-xylosidase had no activity in normal cells, but had measurable activity in virus-transformed cells. Virus-transformed cells had about 1.9 times the proteolytic activity of normal cells; the transfer of N-acetylglucosamine onto glycoprotein acceptors (endogenous or exogenous) was markedly increased in virus-transformed cells. Apparently, the abnormal N-acetyl glucosamine residues found in polyoma virus-transformed hamster kidney cells may be a result of either or all of the following factors: increased proteolytic activity, increased glycosidase activity or increased transfer of N-acetylglucosamine onto glycoprotein on the cell surface.

- 1115 PLAQUE ASSAY TECHNIQUES FOR MURINE LEUKEMIA VIRUSES. (E.) Rowe, W. P. (Natl. Inst. Allerg. Infect. Dis., Bethesda, Md.), W. E. Pugh and J. W. Hartley. *Virology* 42(4):1136-1139, 1970.

See also:

- * (Rev): 0837, 0864, 0866, 0867, 0870, 0875, 0882
- * (Chem): 0953
- * (Phys): 1002
- * (Immun): 1117

- 1116 IMMUNOSUPPRESSIVE EFFECT OF SURGERY. (E.) Park, S. K. (Grad. Hosp. U. Pennsylvania, Philadelphia), J. I. Brody, H. A. Wallace and W. S. Blakemore. *Lancet* 1(7689):53-55, 1970.

The comparative immune reactivity of peripheral blood lymphocytes obtained from surgical patients was investigated to determine the effect of surgical procedures on immunological competence. DNA synthesis, as measured by the incorporation of ^{14}C -thymidine under phytohemagglutinin stimulation, was assayed in lymphocytes grown in cell culture in autologous plasma, in normal lymphocytes from surgical patients grown in plasma from unoperated normal patients. Surgical procedures performed on the test patients included cholecystectomy, cardiac valve replacement, esophagectomy for esophageal carcinoma, abdominoperineal resection and hysterectomy. All patients exhibited depressed immunological competence following surgery, as evidenced by a diminished ability to incorporate radioactive thymidine. Immunological depression was most severe in patients undergoing cardiac surgery for aortic insufficiency, and in patients undergoing pneumonectomy and esophagectomy for carcinoma. In the carcinoma patients, post-operative values for ^{14}C -thymidine uptake were 0.6% and 1.2% of preoperative levels for pneumonectomized and esophagectomized patients, resp., 2 hr post-operatively. While patients undergoing other operations recovered immunological competence by 7 days after their operations, these patients' thymidine incorporation at 7 and 6 days post-operatively were only 19 and 36% of normal, resp. The acceleration of metastasis which often occurs post-operatively in carcinoma patients may be explained by the suppression of immunocompetence associated with the surgical ordeal.

- 1117 TUMOUR DEVELOPMENT FOLLOWING IMMUNOSUPPRESSION. (E.) Allison, A. C. (Natl. Inst. Med. Res., London, England). *Proc Roy Soc Med* 63(10):1077-1080, 1970.

The effect of restoration of immunity on viral induction of tumors was investigated in mice. Female mice were thymectomized and maintained on injections of rabbit anti-lymphocytic globulin for 10 days, at which time they were given i.p. injections of 10^5 TCID₅₀ polyoma virus. Subsequently, some of the mice were given spleen cells from normal mice, and some were given spleen cells from polyoma virus-infected mice (10^6 cells/g wt of recipient) to restore tumor immunity. Eight wk later, all of the unrestored mice, and all but 1 of the mice restored with normal spleen cells had developed tumors: tumors were mammary adenocarcinomas in all but 2 cases. None of the mice given polyoma virus-sensitized spleen cells developed tumors. In a related experiment, 18 mice with small mammary tumors had their tumors excised; mice were then given 5×10^5 polyoma-sensitized syngeneic spleen cells, and the remaining 9 were left untreated. All mice in the untreated group developed tumors, while only 1 of the mice given virus-sensitized spleen cells developed tumors. These results appear to demonstrate that the main factor allowing polyoma virus oncogenesis in thymectomized rats is suppression of cell-mediated immunity.

- 1118 MALIGNANT TUMORS FOLLOWING IMMUNOSUPPRESSIVE THERAPY. (E.) Pritzker, K. P. H. (Path. Inst., McGill U., Montreal, Quebec, Canada), S. N. Huang and K. G. Marshall. *Canad Med Ass J* 103(13):1362-1365, 1970.

Malignant disease associated with renal transplantation and immunotherapy was observed in 2 cases. In 1 case, a 27-yr-old Chinese male received a kidney transplant 4 yr before his death; immunosuppressive therapy (prednisone and azathioprine) was administered intermittently throughout the course of the patient's observation. Autopsy revealed a leiomyosarcoma of the bowel metastatic to the liver. In the other case, a 38-yr-old female received a kidney transplant and immunosuppressive therapy (antilymphocyte serum, prednisone and azathioprine). Six months after the transplantation, carcinoma *in situ* of the cervix uteri was diagnosed. It was thought that a causal connection between immunosuppressive therapy and cancer was probable in the first case and circumstantial in the second. The incidence of neoplasms in immunologically suppressed patients is evidently higher than in other groups, and it appears that immunosuppressive therapy sufficient to allow survival of an allogenic graft may well be sufficient to allow development of spontaneous tumors which are less antigenic than grafts.

- 1119 ANTIBODY-PRODUCING CAPACITY IN HUMAN CANCER. (E.) Lee, A. K. Y. (Walter Eliza Hall Inst. Med. Res., Victoria, Australia), M. Rowley and I. R. Mackay. *Brit J Cancer* 24(3):454-463, 1970.

The ability to produce antibodies to flagellin from *Salmonella adelaide* was tested in 61 patients with cancer and 2 sets of matched controls, one of hospital patients with non-malignant diseases and one of healthy patients. Of 61 subjects, 27 were designated "active" cancer cases, having non-lymphomatous malignancies; 34 patients in the "cured" group had been successfully treated for malignant disease with surgery and/or radiotherapy. All subjects were given s.c. injections of 5 mg of flagellin. Natural antibody to flagellin (IgM class) was found in 84% of active cancer patients, in 93% of cured patients, and in 96% of controls. In active cancer patients, the mean peak titer for total antibody 2 wk after injection of flagellin was 342, compared to a mean peak titer of 1002 for hospital controls. Ten wk after injection with flagellin, IgG antibody titers in controls were at 1.5 (log₁₀ titer) for controls and 0.5 for cancer patients. In 13 cancer patients who survived for more than 6 months after injection of flagellin, the mean peak titer for total antibody was 420, compared to titers of 820 for hospital controls; IgG antibody titers for these 2 groups were 8 and 86, resp. For 14 patients who survived less than 6 months after injection, mean peak titers for total and IgG antibody were 276 and 15, resp., compared with total antibody and IgG titers of 1190 and 57, resp., for hospital controls. Antibody-producing capacity for patients regarded as "cured" by surgery and/or radiotherapy was significantly greater than it was in hospital controls, but significantly less than in healthy controls. The findings may be explained

by an immunodepressive effect specific for cancer or associated with general debility, or by the occurrence of cancer preferentially in those with impaired immunocompetence.

- 1120 ANTIGENIC CHARACTERS IN SPONTANEOUS CELL CARCINOGENESIS. (E.) Vernekar, S. D. (Cancer Res. Inst., Tata Mem. Ctr., Parel, Bombay), S. G. Gangal and K. J. Ranadive. *Indian J Exp Biol* 8(1):11-14, 1970.

The antigenicity of a line of mouse fibroblast cells which exhibited spontaneous transformation (line C3HFB₁) was investigated. For antigenic analysis, the cell line was divided into 4 phases: primary cultures of fibroblasts in the second passage; non-malignant cells up to passage 40 showing morphological transformation; transformed, malignant cells at the 50th passage; and fresh trypsinized embryonal cells (controls). Tanned red cell agglutination and complement fixation tests were used for studying the antigenic constitution of cells. Antisera were prepared in rabbits against all 4 different cell types. The cells appeared to lose some embryonal antigens during the early stages of cultivation. Transformed, nonmalignant cells showed the presence of modified antigens after 20 passages, and the malignant cells at passage 50 showed antigenic similarities to the embryonal cells. The antigenic similarity of malignant and embryonal cells suggest that continuous stimulation to growth and transformation *in vitro* may have hastened the process of antigenic derepression.

- 1121 HUMAN THYMUS-LYMPHOID TISSUE ANTIGEN AND ITS PRESENCE IN LEUKAEMIA AND LYMPHOMA. (E.) Yata, J. (Karolinska Inst., Stockholm, Sweden), G. Klein, N. Kobayashi, T. Furukawa and M. Tanagisawa. *Clin Exp Immunol* 7(6):781-792, 1970.

An antigen associated with leukemias, lymphomas and various lymphoid tissues was demonstrated by immunodiffusion tests with tissue homogenates using an antiserum prepared by immunizing rabbits with human leukemic tissue homogenate following preliminary induction of tolerance to normal peripheral leucocytes by repeated injections. In gel diffusion precipitation tests, positive reactions to the putative antigen were found for all undifferentiated leukemic cells and all myeloblastic leukemia cells. Positive reactions were also found for 67% of malignant lymphoma cells tested, for Burkitt's lymphoma, for postnasal space carcinoma, for thymoma, and for papilloma of the vocal cords. Thymus homogenates from patients dead of nonmalignant diseases also gave positive reactions, as did the spleen and lymph nodes. There was no antigen reaction for extracts of normal non-lymphoid tissue. The antigen could be demonstrated in fetal thymus at 3 months of gestation. In spleen and lymph nodes, the antigen appeared later and less constantly than in the thymus. The antigen was located in the cytoplasm of nearly 100% of thymocytes, about 30% of spleen cells, and 30% of peripheral lymphocytes by the fluorescent antibody method. No antigen could be

demonstrated in bone marrow, brain, thyroid, liver or kidney cells.

- 1122 CHANGES IN THE LYMPHOID SYSTEM FOLLOWING THE INTRAVENOUS INJECTION OF PHYTOHEMAGGLUTININ IN MICE: A PILOT STUDY. (E.) Hartveit, F. (Dept. Path., U. Bergen, Norway). *Acta Path Microbiol Scand* 78(5):525-531, 1970.

The effects of i.v. injection of phytohemagglutinin (PHA) on lymph nodes, spleen and thymus were investigated in male mice. PHA was injected in a saline solution at a concentration of 1.7 mg/ml (approximately 68 mg/kg body wt). Twenty-four hr after injection, lymph nodes were enlarged, soft and microscopically edematous, with marked proliferation of the follicles. Pyroninophilic cells were seen in the germinal centers, paracortically and in the medullary cords. Mast cells in the sinuses were in the process of degranulation. By 6 days post-injection, extra-medullary hematopoiesis was present to a minor degree in most nodes, and some germinal areas showed necrosis. After 11 days, swollen medullary cords had shrunk somewhat, and cellular recovery was evident. Spleen wt of PHA-treated animals increased nearly 2-fold (121 mg in treated animals, 71 mg in normals), and scattered groups of cells appeared which were intensely pyroninophilic. By 2 days post-injection, follicles were markedly enlarged; however, recovery seemed complete by day 11. Few changes were noticed in the thymus of PHA-treated animals; however, the cortex showed active proliferation with large pale pyroninophilic cells. The regular proliferation noted in the lymph nodes may have been due to stimulation of the lymphoid cells *in situ*, while the larger grossly irregular proliferation found in particular lymph nodes may have been caused by secondary stimulation of this altered cell population by PHA-stimulated cells from the thymus.

- 1123 LYMPHORETICULAR MALIGNANCIES AND IMMUNOLOGIC ABNORMALITIES IN A SIBSHIP. (E.) Potolsky, A. I. (332 Oxford Ave., Palo Alto, Cal.), C. W. Heath, C. E. Buckley III, and D. T. Rowlands, Jr. *Amer J Med* 50(1):42-48, 1970.

Immunological studies were performed on 4 sibs surviving from an original sibship of 12 individuals, 5 of whom had died of lymphoreticular malignancies, and 3 of other causes. Of the 5 dying of lymphoreticular malignancies, 2 had chronic lymphocytic leukemia, 1 had lymphocytic lymphoma, 1 had acute leukemia, and 1 had reticulum cell sarcoma. In 1 of the 4 surviving sibs, a 68-yr-old woman, moderately enlarged lymph nodes were observed in the neck, and biopsy revealed changes consistent with lymphosarcoma. All 4 sibs showed clear abnormalities in immunologic tests. Each had decreased immunoglobulin (IgG) levels, and each showed depression in delayed hypersensitivity skin test responses. One individual showed an increased level of immunoglobulin IgM, a decreased level of anti-B isoagglutinin (1:16), and a slight increase in alpha₂-globulin. The patient with signs of lymphosarcoma showed de-

creased levels of IgA and IgM, a slight decrease in gamma globulin and total protein, decreased lymphocyte responsiveness to phytohemagglutinin, an increased number of lymphocytes in bone marrow, and an absence of lymph node germinal centers. All sibs had normal chromosome numbers and karyotypes, with no evidence of increased chromosomal breakage. No evidence of virus was found in any of the sibs. The findings suggest a genetic relationship between immunologic abnormalities and susceptibility to lymphoid neoplasia.

- 1124 HYBRID CELL LINE FROM A CLONED IMMUNOGLOBULIN-PRODUCING MOUSE MYELOMA AND A NON-PRODUCING MOUSE LYMPHOMA. (E.) Mohit, B. (Clin. Ctr. Natl. Inst. Hlth., Bethesda, Md.) and K. Fan. *Science* 171(3966):75-77, 1971.

Hybrid cells were produced by fusing cloned mouse myeloma cells which produced immunoglobulin and cells of a mouse lymphoma originally induced by 7,12-dimethylbenz(a)anthracene which did not produce immunoglobulin. The myeloma was resistant to 8-azaguanine, and produced γ G and free kappa chain immunoglobulins; the lymphoma was resistant to bromodeoxyuridine. Fusion of the parent cell lines was effected with 10^7 cells of each parent line and 2000 hemagglutination U of Sendai virus inactivated by β -propiolactone. After 2 wk in culture, the hybrid cells showed many fused giant cells, and after 6 wk, hybrid cells began to divide and increase in number. The hybrid cells generally had the sum of the chromosome numbers of the respective parent lines. Although no synthesis of α G heavy chain proteins was observed in the hybrid cells, they contained the membrane antigens of both parents, and synthesized free kappa chain proteins. The lack of heavy chain protein synthesis in hybrid cells may have been due to interference with its synthesis during either transcription or translation, possibly by means of a repressor or other control molecules contributed by the non-immunoglobulin-producing parent cell line.

- 1125 THE ROLE OF THE REGIONAL LYMPH NODES IN THE DEVELOPMENT OF HOST IMMUNOLOGICAL RESPONSE TO TUMORS. (E.) Pilch, Y. H. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), D. S. Bard and K. P. Ramming. *Amer J Roentgen* 111(1):48-55, 1971.

The role played in host resistance to tumors by regional lymphatics and lymph nodes was investigated. Normal and tumor-bearing mice (which had been injected with fibrosarcoma cells) were given combinations of the following treatments: right regional lymphadenectomy, sham lymphadenectomy, amputation of the tumor-bearing limb. The size and incidence of tumors developing in these groups was observed. Practically no difference in mean tumor volumes, tumor incidence, or mortality between any of the treatment groups was found, suggesting that removal of regional lymph nodes does not interfere with the host's response to a primary tumor transplant. Removal of regional lymph nodes does not seem to affect the host's ability to resist further tumor growth.

- 1126 IMMUNOLOGIC CROSS-REACTION BETWEEN HUMAN LEUKEMIC PLASMA AND AVIAN LEUKOSIS GROUP-SPECIFIC ANTISERUM. (E.) Cohen, S. (Wayne St. U. Sch. Med., Detroit, Mich.), L. M. Weiner, C. A. Baechler and C. S. Stulberg. *Proc Soc Exp Biol Med* 135(3):800-803, 1970.

Plasma from a patient with acute monomyelogenous leukemia was subjected to immunodiffusion tests with antiserum prepared from a hamster bearing fibrosarcomas induced by Rous sarcoma virus. Plasma from the patient gave at least 2 precipitin bands with the hamster serum. One of the bands merged in a reaction of identity with precipitin bands formed by avian leukosis virus. The leukemia patient's plasma also contained virus-like particles measuring 46-56 nm and were not seen in any of the normal plasmas studied. The particles estimated to be concentrated in amounts of 5×10^7 /ml of plasma; 20% of the particles were in the doughnut form. The reaction of the leukemia plasma with the hamster antiserum apparently represented a genuine cross-reaction between antigens from a human leukemic source and antibodies directed against the avian leukosis group-specific antigen.

- 1127 SHARING OF INDIVIDUAL ANTIGENIC DETERMINANTS BETWEEN A γ G AND A γ M PROTEIN IN THE SAME MYELOMA SERUM. (E.) Penn, G. M. (Rockefeller U., New York, N. Y.), H. G. Kunkel and H. M. Grey. *Proc Soc Exp Biol Med* 135(3):660-665, 1970.

An attempt was made to isolate two lambda proteins from the same human myeloma serum and to determine the nature of antigenic specificity through plasma-phoresis and immunoelectrophoresis. Two proteins, one a γ M and the other a γ G3, were isolated and were shown to have only lambda light chains. They were also shown to share individual antigenic specificity with localization pointing to the light chains and the variable regions of the heavy chains. This sharing strongly suggests that a segment or the entire variable region of the two proteins are markedly similar.

- 1128 IgM DYSPROTEINEMIA AND ACUTE MYELOMA. (PLASMOCYTIC RETICULOSARCOMA OF THE BESSIS AND SCEBAT TYPE.) (It.) Pratesi, G. (Hosp. San Giovanni, Rome, Italy), A. Alfieri, L. Barbatano and A. Fremiotti. *Recent Progr Med* 49(3):xxi-xxxviii, 1970.

A case of acute myeloma with hepatosplenomegaly and an IgM and IgG dysproteinemia in a 64-yr-old woman is presented. The heavily prevalent IgM fraction constituted 33% of the total serum proteins. The cytology of the bone marrow (sternal puncture) revealed a plasmocytic reticulosaoma with atypical plasmocytic elements with giant nuclei or double nuclei with enlarged nucleoli and decreased cytoplasmic contents. The peripheral blood revealed large flattened cells and reticular elements indicating a tendency towards the plasmocytic development. The ambiguous origin of the IgM and IgG producing cells is analyzed in terms of the possibility that a single cell could produce under certain conditions two types of immunoglobulins.

he described case seems to confirm that no precise relationship between the morphology of a proliferating cell and the production of a specific type of immunoglobulin exists.

- 29 EVIDENCE FOR ANTIGENICITY IN HUMAN TUMOURS WITH REFERENCE TO BOTH MELANOMA AND ACUTE LEUKEMIA. (E.) Fairley, G. H. (St. Bartholomew's Hosp., London, England). *Brit Med J* 4(5733):483-34, 1970.

Antigenicity in human tumors was investigated in patients with melanoma and leukemia. It was shown that 86% of the patients with localized melanoma (i.e., patients in whom the disease was confined to the primary anatomical site or to the primary site and the regional lymph nodes) had autoantibodies to melanoma, while only 11% of patients with disseminated disease had antibodies. Antibodies disappeared in 3 melanoma patients when the disease became widespread. However, patients with generalized melanoma produced antibodies when injected with more than 300×10^6 radiation-inactivated tumor cells. While the antibodies may have little effect on massive tumors, they may inhibit metastases. The evidence that there exists a host immune resistance to acute leukemia includes the fact that there are on record 103 cases of people with the disease who are alive and symptom-free 5-17 yr after the onset of symptoms. It was found that leukemic blast cells stimulate autologous lymphocytes, and that tumor-associated antigens exist on the cell surface. Antigenic response to leukemic cells was greater after immunization with autologous irradiated blast cells.

- 30 RELATION BETWEEN BREAST CANCER AND S BLOOD-ANTIGEN SYSTEM. (E.) Boston Collaborative Cancer Surveillance Program, Tufts U. *Lancet* 1(7694):301-304, 1970.

A association was discovered between the phenotype in the S antigen system and breast cancer; the populations examined were breast cancer patients in hospitals in the Boston area. There were 82 breast cancer patients in 1 hospital group and 89 breast cancer patients in the other. Control groups were comprised of patients with cancer in sites other than the breast. In 1 group the proportion of the ss phenotype among breast cancer patients was 61%, while among controls it was 46%. In the other group, 56% of breast cancer patients had the ss phenotype and 41% of controls had the ss phenotype. The point estimate of relative risk for breast cancer in the presence of ss phenotype was 1.8, with 95% confidence limits of 1.2 and 2.7. In addition, the association between ss phenotype and breast cancer was more prominent among patients whose disease had been diagnosed before the age of 50 yr. Despite the excess of ss phenotype among breast cancer patients, there appeared to be a deficit of the phenotype NN in the breast cancer patients relative to controls.

- 31 TUMOR SPECIFIC T-LIKE ANTIGEN OF HUMAN BREAST CARCINOMA. (E.) Taylor, G. (Roy. Infirmary, Manchester, England) and J. L. Odili. *Brit J Cancer* 24(3):447-453, 1970.

An autoimmune response to a neoantigen prepared by fractionation of mammary adenocarcinoma tissue was observed in the serum of 1 patient; in sera of 10 other mammary cancer patients tested no autoantibody response was observed. The antibody response was directed only against the nuclear fraction of the tumor homogenate; there was no response to normal breast tissue in the same individual. When the autoantibody reacting serum was tested against the nuclear fraction of the other 10 mammary adenocarcinomas, tumors from 6 subjects gave positive reactions. That this reaction was specific for mammary adenocarcinoma was demonstrated by the finding that serum prepared from nuclear fractions of adenocarcinomas derived from stomach, rectum, colon, and esophagus all gave negative results when tested against the antibody-containing serum. The nuclear fractions of the 7 mammary adenocarcinomas which apparently shared a common neoantigen were incubated with DNase and RNase, and 6 of the neoantigen were found to be resistant to RNase and were destroyed by DNase; the other neoantigen was inactivated by RNase. The neoantigens appeared to be heat-labile at 37° in pH 7.4 buffer and lost the ability to fix complement after 3-4 hr of incubation under these conditions. Cross absorption also indicated that 2 antigens were present in the sera of the patient with the autoimmune response.

- 1132 DETECTION AND ISOLATION OF TUMOUR-SPECIFIC ANTIGEN ASSOCIATED WITH A SPONTANEOUSLY ARISING RAT MAMMARY CARCINOMA. (E.) Baldwin, R. W. (Cancer Campaign Res. Lab., U. Nottingham, England) and M. J. Embleton. *Int J Cancer* 6(3):373-382, 1970.

Membrane immunofluorescence tests detected a tumor-specific antigen on the surface of a spontaneously arising rat mammary carcinoma. Antisera to the tumor cell lines were prepared in syngeneic rats treated with irradiated (15,000 rads) tumor grafts or with excision of an s.c. tumor mass. Using this antiserum, antigenic reactions were found in 1 of 8 rat carcinomas by membrane immunofluorescence. Fluorescence indices for this antigenic tumor (designated Sp4) had a mean value of 0.36 ± 0.03 . Tumor antigens on Sp4 were individually distinct, and there was no evidence for major common antigens shared by Sp4 and other mammary carcinomas. The capacity of subcellular fractions of Sp4 tumor to absorb anti-Sp4 antibodies was tested. Antibody absorption with amounts of tumor membrane fractions equalling 10-22.5 mg of protein/ml reduced the fluorescence index of anti-Sp4 antiserum to the limiting value for a significant reaction. Absorption of antiserum with Sp4 soluble fraction (91 mg protein/ml) produced no significant loss of anti-Sp4 antibody; membrane fractions of Sp4 absorbed almost all antibodies from an alloantiserum, however. Plasma membrane fractions of Sp4 failed to induce tumor rejection responses when injected into syngeneic rats (100% of rats developed tumors). Sp4 plasma membrane fractions did produce a weak humoral antibody response, however. A weak but consistent humoral antibody response was obtained in rats injected with irradiated tumor grafts.

- 1133 TUMOR-ASSOCIATED IMMUNOGLOBULINS: THE ELUTION OF IgG2 FROM MOUSE TUMORS. (E.)

Ran, M. (Dept. Microbiol., Tel Aviv U., Israel) and I. P. Witz. *Int J Cancer* 6(3):361-372, 1970.

The amount of immunoglobulin IgG2 found in eluates of tissue preparations of primary and transplanted mouse tumors was analyzed semi-quantitatively. Tumors were fibrosarcomas induced in mice by s.c. or i.m. injections of 0.2 ml benzo(a)pyrene. Low amounts of IgG2 were found in eluates of sediments from low-speed centrifugation of cells. Only 0-6% of the total IgG2 units eluted from all sub-cellular fractions of tumor cells was eluted from low-speed sediments. Medium-speed sediments yielded higher IgG2 contents (14-31% of total IgG2). Membrane-rich, high-speed sediments were invariably richest in elutable IgG2, yielding up to 78% of total IgG2. Relatively large amounts of IgG2 could also be eluted from the high speed sediments of spontaneous mouse mammary tumors, indicating that the immunoglobulin is associated with the surface of the tumor cells. No IgG2 could be eluted from high speed sediments of normal muscle cells; however, IgG2 could be eluted from normal liver cells. IgG2 was elutable in much lower amounts from high speed sediments of transplantable benzo(a)pyrene-induced sarcoma cells than from primary sarcomas. IgG2 appears to be preferentially bound to tumor cells and is not a random contaminant of the cells or of the membrane-rich subcellular fraction.

1134 THE *IN VIVO* SPLEEN RESPONSE TO SHEEP ERYTHROCYTES IN BURSECTOMIZED-IRRADIATED CHICKENS. (E.) Alm, G. V. (Variety Club Res. Ctr., La Rabida-U. Chicago Inst., Ill.). *Acta Path Microbiol Scand* 78(5):641-646, 1970.

The *in vivo* response of the chicken spleen to immunization with sheep erythrocytes was studied in 8-wk-old chicks having undergone bursectomy and/or X-irradiation (600 rads). Sheep erythrocytes were given by injection to selected birds in amounts of 5×10^9 cells/kg body wt. Immunization of irradiated birds increased their spleen wt, while no such increase was observed in irradiated and bursectomized birds. Incorporation of ^3H -thymidine by immunized and irradiated chickens was higher than incorporation by immunized and bursectomized birds (incorporation of ^3H -thymidine expressed as cpm/ 10^6 spleen cells was, resp., 48.16 and 27.91 for the 2 test groups). Plaque-forming cell responses in variously treated chickens were assayed in spleens. Spleens of immunized and irradiated chickens contained more plaque-forming cells than did spleens of immunized, irradiated and bursectomized chickens. The former group showed 548 plaque-forming cells/ 10^6 spleen cells assayed by a direct technique; the latter group showed 25-67 plaque-forming cells/ 10^6 spleen cells. So-called "background" sheep erythrocyte antibody forming cells found in the spleens of unimmunized irradiated chickens were absent in spleens of bursectomized-irradiated birds.

1135 IMMUNOLOGICAL AND SEROLOGICAL INVESTIGATIONS IN PREGNANCY AND GENITAL CARCINOMA. (Ger.) Kadach, D. (Women's Clin., Humboldt U., Berlin, Germany). *Zbl Gynaek* 92(48):1577-1580, 1970.

The immunological relationship of a pregnancy dependent α_2 -globulin detected in sera of some patients with mammary gland carcinomas and a protein detected specifically in the sera of patients with ovarian carcinoma was investigated. Ouchterlony tests were performed with serum or carcinomatous tissue homogenates obtained at surgery from 3 groups of patients: I) 7 with mammary gland carcinoma (10 g tissue samples); II) 10 with uterine carcinoma (5 g tissue samples) and III) 10 with ovarian carcinoma (5 g tissue samples). None of the sera or cancer tissue homogenate samples obtained from group I and II produced any precipitin reaction when tested against rabbit antipregnancy serum, whereas serum from 6 and cancer tissue homogenates from 4 patients with ovarian carcinoma exhibited positive reactions. All positive tests were obtained in cases involving histologically confirmed hormone active tumors which probably originated in the estrogen producing ovarian structures. No relation to the α_2 -globulin was established; the positive reactions seemed to be due to an increase in certain carrier proteins which occurred with the increased estrogen secretion.

1136 CHANGE IN THE TYPE OF RADIATION CELL-KILLING ON HUMAN LYMPHOCYTES AFTER BLAST FORMATION BY PHYTOHEMAGGLUTININ. (E.) Sato, C. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan). *Int J Radiat Biol* 18(5):483-485, 1970.

Cell-death caused by radiation was investigated in human lymphocytes stimulated by phytohemagglutinin (PHA) and in unstimulated cells. Cells were exposed to 150-2000 rads of radiation, and the percent of cells surviving was recorded at 0-100 hr after radiation. Small lymphocytes without PHA began to die 10 hr after 500 rads of irradiation; after 40 hr 95% of these cells were lost. PHA-stimulated lymphocytes survived longer, with cell deaths beginning approximately 40 hr after radiation exposure. PHA-stimulated cells exposed to 150 rads exhibited 55% survival 80 hr after radiation, while cells exposed to 2000 rads exhibited 20% survival at this point. The addition of PHA apparently protected small lymphocytes from early normal interphase death, but changed the type of cell death to one related to mitosis. Mitotic block apparently accounted for more cell loss at lower doses of radiation than did cell death *per se*, with the latter accounting for more cell loss at higher radiation doses.

1137 CHANGES IN THE CARBOHYDRATE METABOLISM OF MITOGENICALLY STIMULATED HUMAN PERIPHERAL LYMPHOCYTES: I. STIMULATION BY PHYTOHEMAGGLUTININ. (E.) Roos, D. (Netherlands Red Cross Blood Transfusion Service, Amsterdam) and J. A. Loos. *Biochim Biophys Acta* 222(3):565-582, 1970.

An investigation into the manner in which energy demands are met in the initial stages of human peripheral lymphocyte mitogenic nonspecific stimulation through incubation with phytohemagglutinin are studied along with the effects of various inhibitors on this activity. Decrease of ATP + ADP was accelerated by phytohemagglutinin during the first 2 hr of

incubation followed by an increase to original levels, whereas phosphate incorporation was significantly higher in phytohemagglutinin stimulated lymphocytes after 180 min of incubation with further increase occurring after 4 hr. Aged erythrocytes responded to adenosine + pyruvate with increased levels of ATP, ADP and 2,3-diphosphoglycerate. Increased production of lactate from 39 to 65 μ moles per 1×10^{10} lymphocytes per hr occurred in the presence of adenosine and pyruvate. Moniodoacetic acid caused the lymphocyte level of glucose-6-phosphate to double during the 1st hr of incubation, and then it remained constant for an hour and then decreased. 2,3-Diphosphoglycerate decreased about 80% within 30 min, and lactate and pyruvate production was completely blocked with no changes observed when phytohemagglutinin was added. Potassium cyanide stimulated lactate production to 90%, phytohemagglutinin, 315%, and the combination of KCN and phytohemagglutinin, 590%, while pyruvate production was slightly inhibited and glycerol production greatly stimulated. *In vitro*, glycolysis is the main energy source for phytohemagglutinin stimulation of lymphocytes since inhibitors of glycolysis (moniodoacetic acid and NaF) completely block this action while cyanide does not.

- 1138 HYDROCORTISONE AND PHYTOHEMAGGLUTININ EFFECT UPON THE RNA SYNTHESIS IN THE AGGREGATE ENZYME OF HUMAN LYMPHOCYTES. (E.) Ono, T. Fac. Med. U. Tokyo, Japan), H. Terayama and K. Sakao. *Life Sci* 9(21):1217-1223, 1970.

The mechanism of phytohemagglutinin (PHA) stimulated RNA synthesis was investigated in aggregate enzymes prepared from nuclei of peripheral human lymphocytes. In the presence of 0.4 M ammonium sulfate, the addition of PHA or hydrocortisone had no effect on RNA synthesis in the lymphocyte aggregate system as measured by the incorporation of 3 H-uridine triphosphate or 3 H-uridine triphosphate into RNA. With or without PHA and/or hydrocortisone, lymphocytes incorporated between 2.0-2.5 mole of cytidine monophosphate/50 μ g DNA. Incorporation of nucleotides was not enhanced by the addition of calf thymus DNA to the incubation mixture or by the addition of PHA or hydrocortisone to aggregate enzymes in the presence of *E. coli* polymerase. Aggregate enzymes prepared from lymphocytes preincubated for 4 hr with PHA synthesized more RNA in the presence of ammonium sulfate than the enzyme from control lymphocytes (3 H-uridine triphosphate incorporation was 3.85 pmole/50 μ g DNA for preincubated cells, and 2.44 in controls). Differences in RNA synthesis between enzymes prepared from preincubated lymphocytes and controls disappeared in the presence of *E. coli* RNA polymerase. Addition of hydrocortisone (100 μ g/ml) and A in the preincubation medium prevented the increase in RNA synthesis in the aggregate enzyme assayed in the ammonium sulfate system. These findings appear to suggest that the PHA-stimulated RNA synthesis in lymphocytes is mainly due to an increase in RNA polymerase activity.

- 1139 URINARY IMMUNOGLOBULINS IN PATIENTS WITH CANCER. (E.) Lindstrom, F. D. (U. Minnesota Hosp., Minneapolis), R. C. Williams, Jr. and A. Theologides. *Scand J Haemat* 7(5):383-388, 1970.

Immunoglobulins in the urine of 63 cancer patients, 33 of which were cancer of the breast and cancer of the colon, were studied. Elevated levels of urinary light chain immunoglobulins were noted in only a few cases, and a marked domination of kappa-type light chains was seen in these cases. Twenty-four hr urine specimens were taken and examined for monoclonal immunoglobulins, primarily of the Bence Jones type. Eight patients with reproductive system or gastrointestinal tract cancers showed elevated levels of light chain immunoglobulins, with kappa light chain values in mg/24 hr ranging from 69-302, IgG values ranging from 0-64, and lambda-type values ranging from 0-59. IgG and lambda immunoglobulin values exceeded zero in 2 and 4 cases, resp. The preponderance of kappa-type light chain immunoglobulins recorded for these patients is similar to observations in leukemia and lymphoma patients; however, these immunoglobulins were apparently not of the Bence Jones type, since they lacked the electrophoretic homogeneity of these proteins.

- 1140 PRODUCTION OF 19S AND 7S ANTIBODIES BY CANCER PATIENTS. (E.) Levin, A. G. (Mem. Hosp. Cancer Allied Dis., New York, N. Y.), M. P. Cunningham, A. K. Steers, D. G. Miller and C. M. Southam. *Clin Exp Immunol* 7(6):839-849, 1970.

Titers of 19S and 7S antibodies produced by cancer patients were compared with titers produced by healthy controls. "7S Antibody" was distinguished by persistence of activity after incubation with mercaptoethanol and rapid elution from a DEAE cellulose column by low ionic strength buffer at pH 7.4; "19S antibody" was distinguished by the opposite characteristics. Cancer patients included patients with epidermoid carcinoma and adenocarcinomas, and patients with Hodgkin's disease, lymphocytic leukemia and myeloma. Antibody titrations were determined after injection of 17D yellow fever live virus vaccine. Antibody titers were similar in cancer patients and in controls. At 1 and 2 wk after injection of yellow fever vaccine, mean titers of 7S antibody were less than 1:10 for all subjects; by 4 wk, titers for carcinoma patients were at 1:80, while titers for controls and lymphoma patients were both at 1:20. Titers of 19S antibody were negligible in all groups until about 1 wk after injection with vaccine; by 3 wk, however, controls, carcinoma patients, and lymphoma patients had titers of 3, 2, and 1.5 tubes of 2-fold serum dilutions of decreased antibody titer by mercaptoethanol, resp. By 6 wk after vaccine injection, 7S and 19S antibody titers showed little change in any group. Antibody production was generally delayed somewhat in carcinoma patients; viremia was detected in 1 of 8 controls, in 4 of 20 carcinoma patients and in 2 of 3 lymphoma patients. None of the patients produced interferon.

- 1141 EVIDENCE FOR HUMAN LEUKEMIC ANTIGENS:
ISOLATION AND PARTIAL PURIFICATION. (Fr.)
Viza, D. (Searle Res. Lab., High Wycombe, England),
D. A. L. Davies, R. Todd, O. Bernard-Degani, C.
Bernard and R. Harris. *Presse Med* 78(51):2259-2264,
1970.

See also:

- 1142 IMMUNOLOGICAL ASPECTS OF CANCER. (E.)
Anonymous. *Brit Med J* 4(5733):443-444,
1970.

- * (Rev): 0839, 0849, 0841, 0843, 0883
- * (Chem): 0894, 0904, 0942, 0943, 0956
- * (Viral): 1022, 1036, 1042, 1050, 1054, 1062,
1067, 1072, 1077, 1097, 1104, 1113
- * (Path): 1150

143 NEOPLASTIC CONVERSION *IN VITRO* OF MOUSE CELLS: CYTOLOGIC, CHROMOSOMAL, ENZYMATIC, GLYCOLYTIC AND GROWTH PROPERTIES. (E.) Sanford, K. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), B. E. Barker, R. Parshad, B. E. Westfall, M. Woods, J. L. Jackson, D. R. King and E. V. Peppers. *J Nat Cancer Inst* 45(6):1071-1096, 1970.

Presumably virus-free ALBM-2 mouse embryo cells were observed for progression of cytologic changes, growth-pattern change, glycolytic alteration capacity and inhibitor response indicative of spontaneous changes occurring with neoplastic conversion. Three lines of cells in horse serum had undergone neoplastic conversion by approximately 145-164 days, with latent periods averaging 14 days; a lower incidence of tumors and latent periods averaging 73 days occurred in cells cultured in fetal calf serum. An increase in cytoplasmic basophilia as one of the earliest cytologic changes associated with neoplastic conversion. Neoplastic cells had a high nuclear-cytoplasmic ratio, and the basophilic cytoplasm was densely filled with free ribosomes and polysomes. No changes in enzyme activity could be correlated with neoplastic conversion. Increases in rates of anaerobic glycolysis with time were seen in cells maintained on horse serum but not in cells in fetal calf serum; the former were also less sensitive to glycolytic inhibition by a specific anti-insulin (anti-hexokinase) inhibitor than the latter. The other characteristic change associated with neoplastic conversion was higher saturation density than normal cells and a tendency for cells to adhere less tightly to the glass substrate. Reduced substrate dependency, rather than loss of contact inhibition of mitosis, may account for some of the changes observed in neoplastic conversion of cells under specific culture conditions.

144 THE ULTRASTRUCTURAL DISTRIBUTION OF SEVERAL PHOSPHATASE ENZYMES IN MOUSE MAMMARY TUMOR (STEM. (E.) Misfeldt, D. S. (U. Oregon Med. Sch., Portland), R. D. Cardiff and S. R. Wellings. *Lab Invest* 23(6):640-648, 1970.

The distribution of 3 phosphatase enzymes in tissues representing various stages in the development of a mouse mammary adenocarcinoma were investigated. Nucleoside phosphatase, thiamine phosphatase, and acid phosphatase were assayed in prelactating mammary tissue, lactating mammary tissue, mammary hyperplastic nodules, mammary hyperplastic outgrowths, and mammary adenocarcinoma. Nucleoside phosphatase reaction products were found on the basal and lateral membranes of cells in all 6 tissue-stage samples, while reaction products were found on apical cell membranes only in hyperplastic outgrowth cells and adenocarcinoma cells. Most enzyme observations were made by electron microscope cytochemistry. Control mice without evidence of tumor development showed no evidence of reaction products in the absence of enzyme capture agents or enzyme substrates. The ultrastructural distribution

of all enzyme products was identical in prelactating and lactating mammary tissues. Distribution of nucleoside phosphatase reaction products in normal ductal tissue outgrowths was similar to the distribution in lactating mammary epithelium, with the product distributed along the basal and lateral cell membranes. In hyperplastic alveolar nodules, nucleoside phosphatase was distributed as it was in prelactating and lactating mammary tissue; however, reaction products of this enzyme in hyperplastic nodule outgrowths thought to be of high tumorigenic potential were distributed in the apical cell membranes to a greater extent than was observed in more benign hyperplastic nodules. The apical microvilli were the site of nucleoside phosphatase reaction products in adenocarcinoma cells, again contrasting with the distribution of reaction products among more benign cells where they were more often found on basal and lateral cell membranes. Acid phosphatase was distributed similarly in tissues undergoing nodulogenesis and tumorigenesis. Thiamine phosphatase, present along the basal cell membranes in lactating cells, was absent from the basal cell membranes in adenocarcinoma cells. In tumor cells, nucleoside phosphatase was found in vacuoles associated with virus-like type A particles. The findings appear to indicate that changes in enzyme activity in cell surface membranes preceded tumorigenesis.

1145 PATHOGENESIS AND HORMONAL PROPHYLAXIS IN EXPERIMENTAL DYSHORMONAL DISEASES OF MAMMARY GLANDS. (Rus.) Dmitriev, V. N. (Izhevsk Med. Inst., USSR). *Biull Exp Biol Med* 70(11):90-92, 1970.

The role of sex hormones in the development of mammary gland tumors was studied in 466 randombred female mice. The effect of testosterone and ovariectomy was investigated in 191 mice subjected to continuous electric light exposure (75-200 watt) during the whole experimental period and in 155 mice subjected to synestrol treatment (200 mg s.c., once a wk). Ovariectomy was performed 2 wk before the start of the experiment and testosterone (0.4 mg once a week) was given starting from the 1st day of the experimental period. The effect of testosterone was also studied in a group of 120 mice treated with dimethylbenzanthracene (DMBA, 1 mg in 0.2 ml peach oil injected into the right mammary gland once). Hyperplasia and tumors developed in 90% of the control animals exposed to electric light; prophylactic testosterone treatment or ovariectomy prevented tumor development and decreased the incidence of hyperplasia (8.6% and 15%, resp.) The administration of synestrol induced hyperplasia and tumor development in 95% of the mice in the second experiment. Testosterone treatment and ovariectomy prevented tumor development and decreased the incidence of preneoplastic conditions to 48% and 45%, resp. DMBA induced hyperplasia in 70% of mice, squamous epithelial or adenocarcinoma in 17% and sarcoma in 12% of the animals. Testosterone prevented cancer development and decreased the incidence of hyperplasia to 18%, increasing the life span of the experimental animals an average of 9 wk. The basic endocrine alterations in all experimental groups seemed to be related to variations in follicle stimulating hormones and estrogens.

- 1146 CYTOGENETIC STUDIES IN MYELOPROLIFERATIVE DISORDERS DURING TRANSFORMATION INTO LEUKAEMIA. (E.) Jensen, M. K. (Gentofte Hosp., Copenhagen, Denmark) and P. Philip. *Scand J Haemat* 7(5):330-335, 1970.

Two female patients aged 68 and 79 yr-old with myeloproliferative disorders, (one of which transformed into leukemia) showed abnormal cytological features on cytogenetic study. Pathology in the first case included retroperitoneal hematoma, myeloblastic and myelocytic proliferation, and numerous megakaryocytes. Pathology in the second case included hypoplastic bone marrow, extramedullary hemopoiesis, and numerous megakaryocytes. In the first case, the bone marrow showed 5 abnormal metaphases out of 50 tested. Metaphases contained 46 chromosomes with 2 supernumerary acentric fragments. Five metaphases showed structural aberrations of the chromosomes including breaks of the chromosome and chromatid material. In a marrow aspirate taken at a later date, 22% of the cells showed these features. In the second case, about 25% of the metaphases contained 44 chromosomes with a chromosome missing in groups C and D; in a marrow aspirate taken at a later date, 80% of the metaphases showed this aberration. Supernumerary acentric fragments were found in 3 of 15 cells with 44 chromosomes. Chromosomal abnormalities were present in erythroblasts as well as in white cells. A clonal evolution of abnormal cells was apparently operating in the second case. It was concluded the abnormal cell lines in patients with myeloproliferative diseases may represent a clone of neoplastic cells.

- 1147 MICROCHROMOSOMES IN HUMAN PRELEUKEMIA AND LEUKEMIA. (E.) Pierre, R. V. (Mayo Clin. Rochester, Minn.), H. C. Hoagland and J. W. Linman. *Cancer* 27(1):160-175, 1971.

Microchromosomes were detected in bone-marrow preparations from 9 patients, 7 of whom had myelomonocytic leukemia, 1 of whom has a preleukemic syndrome which degenerated into acute myelomonocytic leukemia, and 1 of whom remained in the preleukemic phase at the end of the study. In some karyotype preparations, 1 microchromosome was found, and in others, as many as 4. The microchromosomes appeared to be marker chromosomes rather than acentric chromosome fragments. Evidence for this conclusion included the fact that in 4 of the 9 cases observed, microchromosomes similar in number and appearance occurred in each cell division episode. This indicated that the microchromosomes were not fragments, for fragments are unstable and generally are lost after a single cell division. It was also thought that the microchromosomes identified 1 or several clones of leukemic cells.

- 1148 INTERRELATIONS OF THE HISTOLOGIC TYPES OF HODGKIN'S DISEASE. (E.) Strum, S. B. (Sch. Med. U. Chicago, Ill.) and H. Rappaport. *Arch Path* 91(2):127-134, 1971.

The histological evolution of Hodgkin's disease (HD) was investigated in a retrospective study of 81

cases. In 13 cases the initial pretreatment lymph node biopsy section was classified as HD with lymphocytic predominance; a second or third biopsy 0.8-11.6 yr later in 7 of these cases revealed HD with mixed cellularity in 2 cases, HD with lymphocytic depletion in 3 cases, HD with nodular sclerosis in 1 case and 1 case of lymphoreticular type HD. In 48 cases the initial biopsy sections showed features of HD with nodular sclerosis; later biopsies 0.1-17.3 yr later showed HD with mixed cellularity in 3 of these cases and HD with lymphocytic predominance in 1 case. Of 7 cases in which the initial biopsy showed many lacunar cells without band formation, 5 developed into classical nodular sclerosing HD in subsequent biopsies. Of 7 cases classified from the initial biopsy as HD with mixed cellularity, 2 revealed HD with lymphocytic depletion in 0.1-1.6 yr. One of 2 cases of HD with lymphocytic depletion changed to HD with mixed cellularity in 2.5 yr. Four cases in which the initial biopsy could not be classified evolved into HD with lymphocytic predominance, nodular sclerosis, mixed cellularity and lymphocytic depletion, resp.

- 1149 REPORT OF A CASE OF MALIGNANT TRANSFORMATION IN BENIGN MIXED TUMOR OF THE LACRIMAL GLAND. (E.) Riley, F. C. (Mayo Clin., Rochester, Minn.) and J. W. Henderson. *Amer J Ophthalmol* 70(5):767-770, 1970.

A case of malignant transformation in an originally benign mixed tumor of the lacrimal gland was reported. The patient, a woman, first presented in 1929, at which time an orbital tumor was excised which was concluded to be a typical benign mixed tumor of the lacrimal gland. In 1969, the patient returned to the hospital, and a malignant sarcomatous lacrimal tumor was excised. The malignant tumor showed spindle-shaped cells with nuclear atypism. Numerous mitotic figures were present and multinucleated cells were seen. Although epithelial cells in the zone of transition were hyperplastic, no certain evidence of carcinomatous transformation was observed. There was no sign of invasion of the muscle.

- 1150 IMMUNOPATHOLOGY OF ORAL LEUKOPLAKIA. (E.) Lehner, T. (Guy's Hosp. Med. Sch., London, England). *Brit J Cancer* 24(3):442-446, 1970.

In vitro studies of transitional changes from leukoplakia to carcinoma were studied through lymphocyte response to autologous homogenates of leukoplakia and to a number of antigens in addition to the relationship of uptake of ^{14}C -thymidine to the changes in human tissue from oral lesions. Histological examination revealed stimulation of lymphocyte transformation in most cases of homogenates of leukoplakic tissue studied and a negative correlation existing between ^{14}C -thymidine uptake of stimulated lymphocytes and the number of non-pyroninophilic mononuclear cell infiltration. Hyperkeratotic (grade I) tissue appeared to be associated with the highest rate of lymphocyte transformation and the lowest mononuclear cell infiltration, with a decrease in the former and an increase in the

ter as the histological grading progressed towards carcinoma. On the basis of these studies, additional criteria for the assessment of premalignancy may be established relative to depression of lymphocyte transformation and increase in number of pyroninophilic cells at the site of the lesion.

- 51 CANINE PAPILLOMA: PROGRESSION OF ORAL PAPILLOMA TO CARCINOMA. (E.) Watrach, A. (Coll. Vetr. Med., U. Illinois, Urbana), E. Small and M. T. Case. *J Nat Cancer Inst* 45(5):915-920, 1970.

A male beagle was seen at a veterinary clinic with multiple papillomatous growths involving the oral cavity, tongue and anterior part of the pharynx; the dog was killed 8 months after first examination due to continuing growth of the neoplasms and worsening condition. Squamous epithelial cells characteristic of squamous cell carcinoma were found on autopsy in the posterior portion of the right jaw; the lesion consisted of many ramifying cords, nests and strands of squamous epithelial cells. Mitotic activity and anaplasia were not pronounced; in some areas cords of tumor cells invaded the bone. There were no metastases, but the anterior cervical lymph nodes showed a moderately advanced inflammatory reaction. A relationship may exist between the duration and extent of papillomatosis and the appearance of malignant change. It is also possible that the papillomatosis degenerated to squamous cell carcinoma as a result of a breakdown in the immune system.

- 2 THE HISTOLOGY OF THE PRECANCEROUS ALTERATIONS OF THE LARYNX. (Ger.) J. Sugár. *Arch Klin Exp Ohr Nas Kehlkopfheik* 197(2):142-153, 1970.

Precancerous changes in the larynx are described including the hyperplastic forms of chronic laryngitis, pachydermia laryngitis and papillomas in adults. A review of histological findings over 14 years, of precancerous carcinoma of the larynx, from light- and electron microscopic observations, is presented. On the basis of histological diagnosis, of the 252 noncancerous but suspicious changes, 120 were of the pachydermia type, and 51 were papillomas. The chronic laryngitis cases were included in the first category, since they could not be distinguished histologically from the pachydermia. In 8 of 120 of these cases, and 6 of the papillomas, atypical epithelium was seen. Fibromatous polyps were found in 46 biopsy specimens. In 25 cases of suspected carcinoma or borderline carcinoma cell changes were seen of a carcinoma in situ. The precancerous changes reported in the investigation stem predominantly from specimens taken from 50-60 year-old patients. In the electron microscopic examination, intracellular filaments were seen which could be interpreted as the precursors of cornification. Changes could also be detected in the cytoplasm of the parabasal and energy layer of the membrane, in the form of extracellular invasion. Basal membrane splits of a 0.1

to 0.5 μ diameter were seen through which the cytoplasm reached the connective tissue.

- 1153 PULMONARY CANCER LOCATED ON CICATRIX. (It.) Ajello, L. (Inst. Anat., U. Rome, Italy) and L. Scorretti. *Policlinico* 77(48):1551-1564, 1970.

The role of cicatrization foci in the pathogenesis of lung cancer is illustrated by 13 case reports. The sclerotic foci originating from tubercular cicatrization and localized in the apical region of the lung seemed to undergo a high incidence of neoplastic transformation. Malignant proliferation occurred when these lesions were exposed to specific conditions of biological susceptibility and to persistent chronic irritating stimuli. Long term anoxia of the bronchial cells, accumulation of inhaled carcinogens and their inclusion within the histiocytic elements may constitute contributing factors. In addition to the usually admitted factors contributing to lung carcinogenesis, the pathogenic role of sclerotic foci within the lung parenchyma or the bronchial walls generated from pneumoconiosis (both silica and asbestos-induced) is emphasized.

- 1154 THE RISK OF SUBSEQUENT CANCER DEVELOPMENT IN CAUSTIC STENOSES OF THE ESOPHAGUS. (Fr.) Gaillard, J. (Hosp. Edouard Herriot, Lyon, France), M. Bouchayer and J. P. Haguenaer. *Ann Otolaryng* 87(10-11):637-644, 1970.

Development of esophageal cancer on the site of caustic injury-induced stenosis is illustrated by 4 case reports. Two of the patients suffered accidental burning with potassium hydroxide at the age of 5 and 3 yr and developed esophageal keratinizing epithelioma at age 63 yr and 50 yr, resp. The other 2 cases were exposed to sodium hydroxide burning at the age of 42 and 4 yr and developed similar neoplasms at the age of 72 and 42, resp. The main features of these neoplasias were the causticity of the stenosis inducing agent, the site of their development (approximately 21 cm from the dental arch, the usual site of caustic agent-induced stenoses) and the long latency periods ranging from 29 to 57 yr. The histological features of these keratinized epitheliomas were specific for their origin from scar tissue as opposed to the tumors arising within the mucosal tissues.

- 1155 POLYPOGENESIS OF GASTRIC MUCOSA. (E.) Muto, T. (Fac. Med., U. Tokyo, Japan) and K. Oota. *Gann* 61(5):435-442, 1970.

Histological examinations were conducted on 142 adenomatous polyps of the gastric mucosa obtained from 89 patients who underwent resection of the stomach. The component of these polyps responsible for their protrusion was the proliferation of ducts not connected to the gastric glands. Characteristic features of these polyps included an elongation and dilation of the gastric pits, hyperplasia, budding and branching of proliferating ducts, interstitial

PATHOGENESIS

edema, cell infiltration, and capillary proliferation. An unusual eosinophilic duct pattern was observed in adenomatous polyps and at the edges of ulcers and over erosion scars; these ducts exhibited eosinophilic epithelium with prominent nucleoli, and their cytoplasm was more pyroninophilic than that of normal gastric pit cells. It was speculated that the genesis of adenomatous polyps proceeded through an initial stage characterized by focal hyperplasia of ducts and glands, followed by ductal proliferation culminating in the development of the classic adenomatous polyp.

- 1156 THE OCCURRENCE OF DESMOIDS IN PATIENTS WITH FAMILIAL POLYPOSIS COLI. (E.) McAdam, W. A. F. (Gen. Infirm., Leeds, England) and J. C. Goligher. *Brit J Surg* 57(8):618-631, 1970.

The occurrence of desmoid tumors in patients with familial polyposis coli was reviewed as it is documented in the literature, and 4 new cases were reported. In the literature, there were 89 cases in which desmoids appeared in patients with polyposis coli; the familial nature of the disease was certain in 50 cases, and probable in 10. The 4 new cases were 3 males and 1 female 15-33 yr-of-age. In 1 case, desmoid tumors were found on the abdominal wall 2 yr after the diagnosis of polyposis coli; in another patient, desmoids were found in the stomach 1 yr after a colectomy for polyposis coli; this patient also had osteomas on the lower jaw. The third patient also presented with osteomas on the jaw and developed desmoids on the surgical scar left after colectomy for polyposis. The fourth patient developed a desmoid at the site of a leg fracture; later she underwent colectomy for multiple abdominal neoplasms, and it was found that carcinoma had involved her liver. Desmoids are hard, fibrous tumors occurring usually in the flat muscles of the anterior abdominal wall; they appear to be infiltrating fibromas of fascial and aponeurotic origin.

- 1157 STATISTICAL MODEL OF THE NATURAL HISTORY OF CERVICAL CARCINOMA: II. ESTIMATES OF THE TRANSITION TIME FROM DYSPLASIA TO CARCINOMA *IN SITU*. (E.) Barron, B. A. (Rockefeller U., New York, N.Y.) and R. M. Richart. *J Nat Cancer Inst* 45(5):1025-1030, 1970.

The probability of cervical dysplasia progressing to cervical carcinoma *in situ*, and the time required for this transition were estimated in terms of a statistical model of the natural history of cervical carcinoma derived from age-specific prevalence rates of dysplasia, carcinoma *in situ*, and invasive cervical carcinoma established from a study of 557 women in Barbados, West Indies. This sample was part of a larger population of 11,814 women from Barbados (women in the 20-39 yr age group were over-represented in the larger population). The proportion of women with severe dysplasia rose with increasing age, with 3.9 cases/1000 population in the 20-24 yr cohort, and 7.1 cases/1000 in the 30-34 yr cohort. The highest weighted mean number of dysplasia cases was 0.494 for very mild dysplasia.

The mean time for transition to carcinoma *in situ* from the very mild dysplasia class was estimated as 68.8 months, and transition time from mild dysplasia to carcinoma *in situ* was 37.3 months; transition times from moderate and severe dysplasia to carcinoma *in situ* were 29.4 and 11.5 months, resp. Prevalence rates for all dysplasias and the ratio of mean transition time to total time were found to be concordant. The time of transition to carcinoma *in situ* and probability of transition were associated with the total number of pregnancies, but were not associated with age at first coitus or with age at first pregnancy. In all classes of dysplasia (very mild, mild, moderate and severe) women who had 2 or less pregnancies had higher relative prevalence ratios than women who with more than 2 pregnancies. The statistical model presented appears to be capable of detecting small changes in the transition probabilities and transition times among different subsets of a test population.

- 1158 RESPONSE OF THE RHESUS MONKEY UTERINE CERVIX TO CHRONIC ESTROGENIC STIMULATION. (E.) Graham, C. E. (Yerkes Reg. Primate Res. Ctr., Emory U., Atlanta, Ga.). *Amer J Obstet Gynec* 108(8):1192-1196, 1970.

The replacement of the columnar epithelium in the endocervix of rhesus monkey by stratified squamous epithelium following chronic estrogen stimulation was investigated in young adult female rhesus monkeys. Monkeys were ovariectomized and treated with estrone (1.5 mg/day) for 2-12 wk; another group of intact monkeys were treated with estradiol benzoate (0.023 mg/day for 4 days). At the end of the treatment period, sections from the uterine cervix and from the lower portion of the uterine corpus were prepared for electron microscopy. In intact monkeys showing no evidence of endogenous estrogenic stimulation, there were no detectable stratified elements in the columnar tissue of the lower part of the endocervical canal. Following treatment with estradiol in ovariectomized animals, the cervical stratified epithelium was thickened and fully cornified, and epithelial cells were observed lying immediately beneath the columnar cells of the endocervix. Similar immature stratified elements could be seen in intact monkeys showing evidence of endogenous estrogenic stimulation. In all ovariectomized chronically treated animals, areas of incompletely cornified squamous stratified epithelium occupied much of the surface of the endocervical canal, approaching the junction with the endometrial region after 8-12 wk treatment. Since foci of stratified cells occurred normally throughout the cervical canal in controls, it was concluded that cervical epidermization is not caused by metaplasia of the columnar cells.

- 1159 CHRONIC CYSTIC MASTITIS AND CANCER: A REPORT OF 206 CASES AND THEIR POSSIBLE RELATIONSHIP WITH TWELVE CARCINOMAS. (Fr.) Chardon, C. (Reg. Anti-Cancer Ctr., Nancy, France), A. Varrault, and R. M. Parache. *Bull Cancer* 57(2):251-268, 1970.

206 women 19-63 yr-of-age with chronic cystic mastitis 12 developed cancer of the mammary gland within 4 yr of observation. Two of these cancers probably preceded diagnosis of cystic mastitis, and occurred within 1 yr and 6 cancers developed 2-4 yr after diagnosis. The latter six cases of cancer developed at an average age of 45 yr on the same date that clinical manifestation of chronic mastitis occurred previously. The incidence of mammary cancer was 7.5-fold greater than corresponding populations of French women unaffected by chronic cystic mastitis. Histologically these cancers appeared to be epitheliomas which are usually considered to be a specific result of malignant transformation of cystic mastitis. Evidence to support this evolution is provided by the presence of structures with epithelial hyperplasia exhibiting patterns intermediate between cystic mastitis and neoplastic structures.

50 ATYPICAL EPITHELIAL HYPERPLASIA OF THE FALLOPIAN TUBES IN CASE OF ENDOMETRIAL CARCINOMA. (Ger.) Dallenbach-Hellweg, G. (Mannheim Univ., U. Heidelberg, Germany) and W. Rom. *Klin Wochenschr* 48(23):1426-1427, 1970.

Epithelial hyperplasia of the fallopian tubes was found in 50 postmenopausal women with endometrial carcinoma who had a history of long term estrogen treatment. The tissues examined exhibited cells with enlarged irregular polymorphic nuclei containing large amounts of chromatin; high levels of DNA was contained in the cytoplasm. When compared to the carcinomatous endometrial epithelium, a close similarity between the two hyperplasias could be noticed. The hyperplastic epithelium presented no invasive features; this type of proliferation may have preceded the development of endometrial carcinoma; its stationary character may be due to the particularly long latency period for malignant development, characteristic at this site. Postmenopausal women without endometrial carcinoma had fallopian tubes lined with atrophic epithelium as expected. The hyperplastic alterations at both sites seemed to have been induced by the same hormonal stimulation since both sites are known target organs for estrogens.

1 THE ADENOMATOID TUMOR: FINE STRUCTURAL EVIDENCE FOR A MESOTHELIAL ORIGIN. (E.) McKay, B. (U. Texas M.D. Anderson Hosp. Tumor Inst., Houston), J. L. Bennington and R. W. Skoglund. *Cancer* 27(1):109-115, 1971.

An adenomatoid tumor obtained from the epididymis of a 9-yr-old male presented the appearance of a typical adenomatoid tumor, with numerous thin-walled channels lined by cells having irregular, microvilli-like projections on their luminal surface under light microscope; scattered foci of lymphocytes were seen. Electron microscopy showed that the lining cells were cuboidal in shape with a spherical or ovoid nucleus. Adjacent cells were joined by terminal bars and by elaborate series of desmosomes. Cell cytoplasm included scattered microsomes; and free ribosomes were abundant. There were areas between adjacent cells where apposed cell membranes separated

to form an anastomosing network of secondary channels communicating with the main channel lumens and rarely with stromal space. Within the channel lumens were aggregates of cytoplasmic debris containing disintegrating mitochondria and myelin figures. Round cells which did not resemble any specific blood or connective tissue cells were also present in the channel lumens; these cells may have migrated from surrounding stroma into the channel lumen. The irregular microvilli, the terminal bars joining adjacent cells, the desmosomes, and the appearance of secondary channels suggested that the adenomatoid tumor was of mesothelial origin.

1162 THE PHYSICAL BASIS OF PROTEIN MODIFICATION AND ITS RELATION TO THE PROBLEM OF CARCINOGENESIS. (Ger.) Caro, W. (Phys. Chem. Inst., Humboldt U., Berlin, Germany). *Arch Gesehwulstforsch* 36(2):127-131, 1970.

A type of irreversible protein conformational alteration which seems to have a role in carcinogenesis was investigated. Kinetic determinations on methemoglobin and metmyoglobin (Methb) allowed the derivation of relationships involving native protein (N), S1 (with intramolecular modification), S2 (with intermolecular modification), and their denaturation products DN, DS1, DS2 and rate constants and activation energies EDN, ES1 and ES2. Benzene increased all rate constants and decreased ES1. Extrapolation of Methb-data to 37°C revealed that formation of S1 is equal to 5% after 50 days (the average age of an erythrocyte) and exceeded all the other Methb-modifications. The addition of 0.0027 moles of benzene (a modification enhancing compound) increased the formation of S1 by 12%. The properties of the modified S1-methb compared to N-protein consisted of a 5% increase in helix content (as opposed to protein denaturation) and an increase of phenylalanine side chain van der Waal's linkage; the structure was stable against denaturation, and its environment was not subject to alterations, indicating the maintenance of biological activity; minor shifting in solubility occurred and full maintenance of crystallizing properties was observed. These data seem to indicate that protein modifications, can be enhanced by means of aromatic carcinogens. The possibility that such protein modifications, induced by physical, chemical and viral agents, may constitute part of the etiology of carcinogenesis is reviewed.

1163 RELATIONSHIPS BETWEEN CIRRHOSIS AND LIVER CANCER. AN EXPERIMENTAL STUDY. (Fr.) Robert, P. K. (Hosp. St. Joseph, Paris, France). *Soc Med Paris* 173(6):5-8, 1970.

1164 CARCINOMA ARISING IN AN ANAL FISTULA. (Nor.) Gronmark, T. (Telemark Central Hosp., Norway). *T Norsk Laegeforen* 90(24):2258-2259, 1970.

See also:

- * (Rev): 0842, 0846, 0851, 0852, 0853, 0854, 0860, 0862
- * (Chem): 0926, 0950, 0957, 0983
- * (Viral): 1034, 1040, 1048

- 1165 LIVER CANCER DIFFERENTIALS IN IMMIGRANT AND LOCAL-BORN CHINESE IN SINGAPORE. (E.) Shanmugaratnam, K. (Fac. Med. U. Singapore) and C. Y. Tye. *J Chron Dis* 23(5-6):443-448, 1970.

The differential incidence of liver cancer among immigrant Chinese and local-born Chinese in Singapore was investigated. Ninety-nine cases of liver cancer were examined and compared with 1044 control hospital patients. There were 79 male liver cancer cases and 20 female cases; 68 of the male cases occurred in patients from 40-69 yr. Persons born in China accounted for 73% of the liver cancer patients, and 53% of the hospital controls. The Chinese-born account for 17% of the Chinese population of Singapore. It appeared from the data that immigrant Chinese had a 75% higher risk of contracting liver cancer than local-born Chinese. All the Chinese-born liver cancer patients had resided in Singapore for more than 10 yr; 51% of them had been born in the Kwangtung province of China, and 63% in the Fukien province. The excess in liver cancer cases among Chinese-born immigrants to Singapore is less than that found in previous studies.

- 1166 LEUKAEMIA IN KENYA. (E.) Kasili, E. G. (Med. Res. Lab., Nairobi, Kenya) and J. R. Taylor. *E Afr Med J* 47(9):461-468, 1970.

The incidence of leukemia in the African population of Kenya since 1967 was investigated. Yearly occurrence of the disease showed a fairly constant pattern, 40 cases having been recorded in 1967, 43 in 1968 and 44 (projected) in 1969. The minimum incidence of leukemia was estimated as 3.4 cases/100,000 population based on figures from the Kiambu District; incidence of leukemia in the United States and Denmark by comparison were 8.6 and 8.4/100,000 male population. Males were found to be more susceptible to leukemia in Kenya than females; in the 0-14 yr age group, there were 16 male and 8 female leukemia patients on record, and in the over-15 yr age group there were 50 males and 31 females. Chronic lymphatic leukemia showed the strongest male predominance, the male-female ratio for this condition being 1.80:1.00. The most common type of leukemia in Kenya was acute myelogenous leukemia, accounting for 28 of 104 cases; chronic myeloid leukemia comprised 27 cases, and chronic lymphatic leukemia, 17 cases. Chronic lymphatic leukemias showed higher hemoglobin values than other types of leukemia. Inadequate diagnosis appeared to be an important factor in the low figures for leukemia incidence in Kenya.

- 1167 INCIDENCE OF MALIGNANT NEOPLASMS IN THE CRACOW DISTRICT IN RELATION TO THE PLACE OF LIVING. (Pol.) Kolodziejska, H. (Oncol. Inst. Cracow, Poland). *Nowotwory* 20(4):305-310, 1970.

The average annual incidence of malignant neoplasia in the district of Cracow was 158 in females and 149 in males per 100,000 population according to the available records for 1965-1968. This inci-

dence appeared to be higher within the urban area of Cracow (227 in females and 180 in males) than in the country (177 in females and 150 in males) per 100,000 population. A higher incidence in lung cancer in both males and females was noticed within the urban area (24% and 5%, resp.) than in the country (18% and 4%, resp.). The incidence in gastric cancer appeared to be lower in the urban area of Cracow for both males and females (15% and 8%, resp.) than in the country (26% and 16%, resp.). The incidence of cancer of the cervix was 17% in the urban area and 14% in the country. It is suggested that these differences between cancer incidences in urban and country areas may be due to environmental factors, regardless of the better records available for the urban areas.

- 1168 LIVER CANCER IN BEDOUINS OF THE NEGEV: AN ETIOLOGICAL AND MORPHOLOGICAL STUDY. (E.) Gussarsky, J. (Negev Central Hosp., Beer-Sheva, Israel), M. Gross and G. M. Goldberg. *Path Microbiol* 35(1-3):184-188, 1970.

The pathology of liver tumors discovered in 14 cases in the Negev (Israel) was examined. Though Jews outnumber Bedouins in the Negev by 8:1, 7 of the 14 cases of liver cancer studied were Bedouins. Material was taken from 8 autopsies and 6 biopsies of livers of 7 Bedouin patients (all males) and 7 Jews (2 females). Patients ranged in age from 31-70 yr-old. All livers showed cirrhosis, and all biopsy specimens were diagnosed as hepatocellular hepatoma. Four autopsy cases were hepatocellular hepatomas, and 4 were cholangiocellular hepatomas. Metastases were found in all autopsy cases, with sites of metastases including lungs, lymph nodes, brain and thyroid. The excessive occurrence of liver cancer in Bedouins in this study could not be explained; hepatotoxic agents were excluded, and a racial factor predisposing to liver cancer was suggested.

- 1169 GEOGRAPHIC PATHOLOGY OF ORAL, ESOPHAGEAL, GASTRIC, AND INTESTINAL CANCER IN CHILE. (E.) Zaldivar, R. (Hlth. Res. Inst., Fairleigh Dickinson U. Madison, N. J.). *Z Krebsforsch* 75(1):1-13, 1970.

The incidence and geographic distribution of cancer of the alimentary tract in Chile was investigated in a survey of mortality rate statistics from that country. Cancer of the oral cavity and pharynx accounted for 81 of 7,618 deaths from cancer of the alimentary system in 1960; males made up 51 of these cases. Malignancies of the tongue and pharynx accounted for 18 and 33 of the 81 deaths, resp. Esophageal cancer accounted for 356 of the total alimentary cancer deaths, of which 228 were among males. Death from esophageal cancer was more frequent in northern provinces of Chile than in the southern provinces; the age-adjusted death rates from the northern province of Aconagua was 11.1 deaths/100,000 population, and from the southern province of Bio-Bio, the rate was 0.5/100,000. In all alimentary tract cancers except cancer of the mouth and pharynx and

cancer of the small intestine, the frequency of deaths increased with increasing age, with the number of deaths usually leveling off around age 75-. The age-adjusted death rates for stomach cancer among females in Chile are the highest in the world (12.2 deaths/100,000 population in 1964). The highest death rate for stomach cancer in Chile was 75.8 deaths/100,000 recorded in the central province of Antofagasta in 1962, and the lowest death rate was 18.1 deaths/100,000 in the southern province of Magallanes the same yr. High death rates from alimentary tract cancer were often recorded in agricultural provinces, indicating that a causal relationship may exist between the use of nitrate fertilizers and the incidence of alimentary tract cancer in Chile.

MESOTHELIOMA IN SCOTLAND. (E.) McEwen, J. (Dept. Soc. Occup. Med., U. Dundee, Scotland), Finlayson, A. Mair and A. A. M. Gibson. *Brit Med* (5735):575-578, 1970.

A retrospective survey of mesothelioma cases in Scotland during the period 1950-1967 was performed, and the possibility of an association between mesothelioma and exposure to asbestos was investigated. Eighty cases of mesothelioma were collected, and compared with controls comprised of non-cancer patients with no exposure to asbestos and patients with cancer other than mesothelioma who reported exposure to asbestos. Of the 80 mesothelioma cases, 73 were men and 7 were women; 69 of the men had pleural tumors and 2 had peritoneal tumors, while 6 of the women had pleural tumors and 1 had a peritoneal tumor. Most cases in both sexes occurred in patients in the 50-69 yr age group, and a preponderance of cases were reported from Glasgow and Edinburgh. Ninety-five percent of mesothelioma patients smoked 1-14 g of tobacco/day, while 16% of mesothelioma cases were non-smokers. Ninety-five percent of mesothelioma cases had experienced either definite or probable exposure to asbestos, while 60% of cancer controls had had asbestos exposure, and 30% of noncancer controls had had asbestos exposure. More than twice as many mesothelioma cases reported residential as well as occupational asbestos exposure than did not. Occupational exposure to asbestos in mesothelioma patients was usually incurred in connection with the Scottish shipbuilding industry.

GALLBLADDER CARCINOMA IN THE MEXICAN POPULATION OF THE SOUTHWESTERN UNITED STATES. Bornstein, F. P. (Providence Mem. Hosp., El Paso, Tex.). *Path Microbiol* 35(1-3):189-191, 1970.

The incidence of gallbladder carcinoma in the Mexican population of the El Paso, Texas, area was investigated. In a survey of 4,500 autopsies, there were 94 carcinomas of the gallbladder and bile ducts and 64 carcinomas of the pancreas. In a comparison population from Chicago, there were 23 pancreatic carcinomas and 3 cancers of the gallbladder and ducts. These figures yield age-adjusted incidence rates of 6 cases of gallbladder cancer/100,000 cases in the Mexican population compared to 2.2 cases/100,000 for the non-Mexican population. The incidence rates for the Latin American population show 12 gallbladder cases/100,000 for women and 4 cases/100,000 for men. The high incidence of

gallbladder cancer among Mexican-Americans may be due to the Mexican practice of eating highly spiced foods in a low animal-protein diet.

1172 GASTRIC CARCINOMA IN A FIXED POPULATION: HIROSHIMA AND NAGASAKI. (E.) Yamamoto, T. (Atomic Bomb Casualty Commis. Hiroshima, Japan), H. Kato, K. Ishida, E. Tahara and D. H. McGregor. *Gann* 61(5):473-483, 1970.

The incidence of gastric carcinoma among residents of Hiroshima and Nagasaki, Japan, who had been exposed to nuclear bomb blast-irradiation in 1945 was investigated, and an attempt was made to correlate the degree of radiation-exposure and the subsequent development of cancer of the stomach. Autopsy records from 2,908 cases of carcinoma of the stomach in the exposed population were examined. The prevalence rates of gastric carcinoma in general showed that rates were higher for females in Hiroshima than for females in Nagasaki (prevalences of 9.9 and 5.9% for the 2 cities, resp.). Males showed a prevalence peak around age 50 yr, while prevalence peaks among females occurred around age 40. Seventy-eight percent of fungating lesions were of the papillary tubular type and 37% of the scirrhous type of carcinoma were of the fungating type. More carcinomas were found in the pylorus and fundus areas of the stomach than in other sites (41 and 19% of tumors in the 2 sites, resp.). The frequency of tumors in the fundus was high in subjects under 60 yr and high in the pylorus in subjects over 60 yr. Diffuse carcinomatous proliferation involving the entire stomach was more frequent in cases of scirrhous type carcinoma than in the tubular medullary type carcinoma; tubular medullary type carcinomas were the most common type followed by scirrhous type carcinomas. Metastases were found in the liver, intestinal tract, and pancreas. In general, no significant correlation was found between the prevalence rate of stomach cancer and amount of radiation exposure, except in males in Nagasaki.

1173 THYROID CARCINOMA IN CHILDHOOD: FINAL REPORT ON A 20 YEAR OLD STUDY. (E.) Winship, T. (Child. Hosp., Washington, D.C.) and R. V. Rosvold. *Clin Proc Child Hosp D C* 26(11):327-348, 1970.

The incidence, pathology, and clinical course of 878 cases of childhood thyroid carcinoma collected since 1948 were detailed. Nearly 80% of these cases were reported from the United States, but it was estimated that the case reports comprised less than 1/2 of cases occurring in the United States, and an even smaller fraction of cases occurring throughout the world. The distribution of the cases failed to confirm the hypothesis that thyroid cancer has a high incidence in goiterous areas of the world; highest incidence rates were recorded from Hawaii, Colombia, Israel and Iceland, of which only 2 are goiterous regions. Most recorded cases of thyroid cancer were diagnosed between the yrs 1945-1955 with a peak in 1957 (70 cases diagnosed); thereafter, the number of cases fell off sharply, perhaps reflecting the decline in popularity of radiation therapy given to the heads and necks of

children. A relationship was found between radiation of the head and neck and thyroid cancer; histories of radiation were obtained from 476 patients. Of these, 76% had been treated from 3.5 to nearly 14 yr before the diagnosis of thyroid cancer. Radiation doses ranged from 140-2600 rads. The relationship between radioactive iodine and thyroid cancer was emphasized. The ages of patients in the study for whom complete clinical data was available was 1 wk-14 yr, with the average age being 9.4 yr; 62% of the patients were girls. In 4 instances, thyroid cancer occurred in members of the proband's family. For the most part, presenting symptoms were 1 or more firm painless nodules in the neck; in 9 patients the first evidence of the disease was pulmonary metastases. Seventy-four percent of patients showed metastatic carcinoma in the cervical lymph nodes at the time of first examination. Treatment was usually surgical. Seventy-one percent of the cases of thyroid cancer were of the papillary type, and 17% were of the follicular type. On follow up, it was found that 300 patients survived for 10 yr, 16 survived for 30 yr, and 2 survived for 40 yr.

- 1174 EXPERIENCE WITH 1079 CASES OF CANCER OF THE STOMACH SEEN IN KOREA FROM 1962 TO 1968. (E.) Crane, P. S. (Nashville, Tenn.), S. U. Rhee and D. J. Seel. *Amer J Surg* 120(6):747-751, 1970.

The incidence and pathology of stomach cancer was investigated in a population from Korea; case material included 1,079 cases of stomach cancer admitted to the hospital between 1962 and 1968. The number of cases recorded in this period rose steadily with 87 cases in 1962, 132 in 1964, and 230 in 1968. The stomach cancer patients comprised 1.7% of all patients presenting at the clinic where the study was performed. Seventy percent of the patients were over 45-yr-old, and 53% were over 50-yr-old; the male-female ratio was 3 to 1. The peak age for onset of stomach cancer in males was 52 yr and for females, 42 yr. Sixty-six percent of the sample population was composed of farmers, while 50% of all patients presenting to the hospital were farmers. In 74% of cases, the stomach tumor was located in the pyloric region; 88% of those patients for whom a pathologic diagnosis was made were diagnosed as having adenocarcinoma and anaplastic cancer was found in 10%. A study of the diets of 170 of the patients showed that patients with stomach cancer appeared to have a significantly higher intake of soy bean paste than patients of the same age and sex without stomach cancer. The fact that *Aspergillus flavus* is found in soy bean cakes eaten by Koreans raised the possibility that aflatoxins produced by this mold may have a role in the genesis of stomach cancer in this population.

- 1175 A COMPARISON OF SOME EPIDEMIOLOGICAL ASPECTS OF CERVICAL AND ENDOMETRIAL CARCINOMA. (E.) Modan, B. (Tel Hashomer Govt. Hosp., Ramat Gan, Israel), Z. Sharon, M. Shani and C. Sheba. *Path Microbiol* 35(1-3):192-197, 1970.

The incidence of cancer of the cervix and endometrium in the Jewish population of Israel was investigated. The study group comprised 275 cases of cervical cancer and 388 cases of endometrial cancer; mean annual incidence for the 2 conditions were 4.7 cases of cervical cancer/100,000 population and 6.6 cases of endometrial cancer/100,000. (Although 25 cases were recorded among Arabs, the analyses of the data were performed only on cases recorded among Jews.) For both cervical and endometrial cancer, there are peaks in incidence in the 60-69-yr-old group. While case of cancer of the corpus increased steadily in frequency until the age of 60, the incidence of cervical cancer declined from age 42-52 yr. Forty-four percent of patients with cervical cancer were less than 50 at diagnosis, while 20% of patients with cancer of corpus were less than 50 yr. The rate of cervical cancer was higher among African born Israelis, while the rate of endometrial cancer was higher among European born Israelis. At age 60, African born Israeli had an incidence of cervical cancer of 27%, while at the same age European born Israelis had an incidence of 9%. At age 65, European born Israelis had an incidence of endometrial cancer of 42%, while at the same age, the incidence for African born Israelis was 23%. The excess of cervical cancer among the African-born may be attributable to those born in Morocco, where the ratio of cervical to endometrial cancer approaches 5:1. More women who had been married had cervical cancer, while more single women had endometrial cancer.

- 1176 MALIGNANCIES IN MAINLAND TANZANIA: SQUAMOUS CELL CARCINOMAS. (E.) Anderson, C. (Central Path. Lab., Dar Es Salaam, Tanzania). *Acta Trop* 27(3):208-218, 1970.

The incidence, demographic distribution, and age distribution of squamous cell carcinoma of various sites were investigated in the Tanzanian population. Site distribution of 1527 cases of squamous cell carcinoma showed that only tumors of the skin and of the cervix uteri occurred in sufficient numbers for adequate epidemiological analysis; cancer of the skin was found in 393 males and 256 females, and cancer of the cervix was found in 431 cases. Demographically, the Wayao and Wazaramo tribes had the highest incidences of squamous cell carcinoma of the cervix, showing 7.77 and 4.15 cases/100,000 population, resp. The most common location for carcinoma of the skin was the lower limb (66% of male cases and 67% of female cases). For females, the second common location for skin cancer was the trunk (9% of female cases); and for males, the second most common location was the scalp and neck (11% of male cases). The Wabena and Wagogo tribes had slightly higher incidences of skin cancer than other tribes (2.40 and 2.14 cases/100,000 population, resp.). The age distribution of 115 cases of squamous cell carcinoma of the skin showed a peak in incidence between the ages of 45-50, and a lower peak in incidence between the ages of 60-65.

77 THE EPIDEMIOLOGY OF ORAL AND OROPHARYNGEAL CANCER IN INDIA. (E.) Jussawalla, D. J. *Annals of the Tata Mem. Hosp., Bombay, India. Oto-Rhino-Laryngology* 206:832-839, 1970.

The incidence and mortality of oral and oropharyngeal cancer in India was investigated, and a specific etiological factor identified. Age-adjusted incidence rates for cancer of the buccal cavity and pharynx indicate that the Bombay area has the highest worldwide rates for both males and females (13 and 15 cases/100,000 population, resp.); these rates were markedly higher than rates for Puerto Rico, the nation with the next highest incidence rates (Puerto Rican rates for males and females, resp., were 24 and 9 cases/100,000 population). Incidence rates for cancer of the lip, salivary glands, nasopharynx, buccal mucosa, palate and nasopharynx in Bombay were approximately comparable to rates for other countries; however, females in Bombay appeared to have a slightly higher incidence of lip cancer than males in other countries. Incidence rates for cancer of the tongue and pharynx were higher in Bombay than elsewhere; rates for tongue cancer for males and females in Bombay were 14.6 and 3.3 cases/100,000, compared 7.1 and 2.1 cases/100,000 for males and females in Puerto Rico. Mortality rates for cancer of the buccal cavity and pharynx were higher in Bombay than elsewhere, with Bombay's rate being 2.4 deaths/100,000 population compared with 2.3 deaths/100,000 for Ceylon and 1.3 deaths/100,000 for American Caucasians. Tobacco chewing was identified as an etiological factor in oral and oropharyngeal cancer in India, with 72% of oral and pharyngeal cancer patients being tobacco chewers. Another etiological factor appeared to be abrasion of the back of the tongue by sharp decayed teeth.

78 THE RISING INCIDENCE OF CARCINOMA OF THE PANCREAS: AN EPIDEMIOLOGIC APPRAISAL. Krain, L. S. (Los Angeles, Calif.). *Amer J Roentgenol* 54(5):500-507, 1970.

Environmental and genetic factors in the incidence of cancer of the pancreas were investigated in an examination of mortality rate data for this condition. Age-specific death rates showed that death rates for cancer of the pancreas becomes markedly more frequent after the age of 45 yr and does not level off appreciably before the age of 85 or above; rates per 100,000 population from pancreatic cancer were 8 at the age of 45 yr and 32 at 60 yr. Female death rates from cancer of the pancreas approached male death rates 10 yr after menopause, with female mortality increasing relative to male mortality after the age of 60. The numbers of male and female hospital admissions for pancreatic cancer were 9.6 and 6.4/100,000 population, resp., for Caucasians and 13.0 and 6.0/100,000 population for Negroes. Negro males have the highest incidence of cancer of the pancreas, and Japanese living in America have a higher incidence of the disease than do Japanese living in Japan. The above finding confirms the importance of environmental factors in pancreatic cancer. The observed lack of relationship of the condition to menopausal

or climacteric periods further minimizes a hormonal or genetic linkage for pancreatic cancer and suggests that exogenous factors are more important. Cigarette smokers who consume from 21-39 cigarettes/day were found to have a lower median age of occurrence of cancer of the pancreas than nonsmokers or light smokers. Death rates/100,000 population for smokers are 11 and 19, resp., for females and males aged from 45-65 yr; death rates for nonsmokers in the same age and sex categories are, resp., 6 and 7/100,000 population. An inverse relationship was found between rank order of air pollution in 4 California cities and their incidences of pancreatic cancer; however, differences among cities were insignificant, and it was concluded that air pollution is not as closely related to pancreatic cancer incidence as is cigarette smoking.

1179 CANCER IN IRAN: STATISTICAL REVIEW ON 28,000 CASES. (E.) Habibi, A. (Tadj Pahlavi Cancer Inst., U. Teheran, Iran). *Path Microbiol* 35(1-3):181-183, 1970.

The distribution of cancer of various sites in the population of Iran was investigated in a review of 28,000 cases. Among males, the 3 most frequently occurring types of cancer were cancer of the skin (26% of cases), cancer of the lymph nodes (12% of cases), and cancer of the esophagus (5% of cases). Among females, the most frequently occurring types of cancer were cancer of the cervix (21% of cases), cancer of the skin (16% of cases), and cancer of the breast (13% of cases). Skin cancer was the most common form of malignancy, accounting for 21.7% of total cases. This disease appeared to be causally related to exposure to sunlight, contact with contaminating clothing, and poor personal hygiene; it was more prevalent in the poorer classes of Iranians. Most skin malignancies appeared on the face, head and neck, and most patients with skin cancer were between 50-69 yr-of-age. Cancer of the cervix was the next commonest malignancy in Iran. Most patients were between the ages of 35-54 yr-of-age, and most were from the poorer socioeconomic classes. The frequency of lymphatic cancer was similar in all social classes. Half the cases of lymph node cancer were located in the neck. Hodgkin's disease comprised 40% of the cases of lymphatic cancer. Breast cancer occurred with greatest frequency among women who had not breast-fed children, and was accordingly prevalent among the more leisured classes. Esophageal tumors were more frequent in the middle and lower third of the esophagus; squamous cell carcinoma was very common in connection with esophageal cancer, making up 85% of cases. Cancer of the larynx and lower respiratory tract comprised 5% and 4%, resp., of male cases. Most patients affected with these 2 forms of cancer were between 45-64 yr-old.

1180 NATURAL HISTORY AND TREATMENT OF WILM'S TUMOR: AN ANALYSIS OF 335 CASES OCCURRING IN ENGLAND AND WALES 1962-1966. (E.) Ledlie, E. M. (Dept. Soc. Med., Oxford U., England), L. S. Mynors, G. J. Draper and P. D. Gorbach. *Brit Med J* 4(5729):195-200, 1970.

Clinical features of Wilm's tumor were examined in a survey of 335 cases of this condition. All patients were under the age of 10 yr; there were 184 boys and 151 girls. Peak incidence of tumors was at 18 months of age (70 cases); by 9.5 yr of age, the number of cases had declined to 8. Congenital tumors occurred in 10 children, and congenital defects including duplex kidney and hemihypertrophy were associated with Wilm's tumor in 20 cases. Tumors recurred after nephrectomy in 156 of 232 cases followed after surgery; the 3 yr survival rate for recurrence cases was 12%. Three yr survival for nephrectomized patients was approximately 35%; no patient who did not undergo nephrectomy survived. In some cases, tumors may have been associated with obstetric radiography during the third trimester of pregnancy; latent periods from irradiation to onset of symptoms were from 12-36 months. Pulmonary metastases were noted in 105 cases. Little improvement in survival rate was effected by treatment with actinomycin D.

1181 CERTAIN MORTALITY PATTERNS OF ESOPHAGEAL CANCER IN THE UNITED STATES, 1930-1967.

(E.) Schoenberg, B. S. (Rochester, Minn.), J. C. Bailar, III and J. S. Faumeni, Jr. *J Nat Cancer Inst* 46(1):63-73, 1971.

Mortality rates for cancer of the esophagus were examined for different white and non-white populations in the United States and for different geographic areas. An excess in mortality was found for non-white groups, which included Negro, Chinese and Japanese; mortality rates for Negroes generally exceeded those for Chinese and Japanese. From 1960-1964, average age-adjusted mortality rates/100,000 population for Negro males and females were 9.99 and 2.39, resp., in this period; mortality rates for Chinese men and women were 8.12 and 0, resp., and 6.30 and 0.43, resp., for Japanese men and women. In the same period, mortality rates for the white population were 3.69/100,000 and 0.96/100,000 for males and females, resp. The highest rates of esophageal cancer mortality were recorded from the Northeastern United States, and the lowest rates were recorded from the South. While male whites living in New England had mortality rates of 4.52/100,000 from 1960-1965, whites in the East South Central region at the same period had rates of 2.26/100,000; non-whites in New England over the same period had mortality rates of 14.36/100,000 and non-whites in the East South Central region had a rate of 5.02/100,000 esophageal cancer mortality was correlated with urbanization, cigarette sales, and alcohol sales. Some factor other than smoking or alcohol consumption was presumed to be operating in the urban environment which predisposed its city dwellers (especially non-white city dwellers) to cancer of the esophagus.

1182 PET ASSOCIATION WITH SELECTED HUMAN CANCERS: A HOUSEHOLD QUESTIONNAIRE SURVEY.

(E.) Hanes, B. (Dept. Hlth. Sci., San Fernando Valley St. Coll., Northridge, Cal.), M. B. Gardner,

C. G. Loosli, G. Heidebreder, B. Kogan, H. Marylander and R. J. Huebner. *J Nat Cancer Inst* 45(6):1155-1162, 1970.

The hypothesis that persons with specific types of cancer known to be associated with C-type viruses in cats might have more exposure to domestic cats than healthy control groups was investigated. A questionnaire survey was conducted among households of victims of leukemia, lymphoma, or sarcoma, and among control households; 530 "index" cancer households and 1,042 control households were included in the survey. It was found that the average yr of cat ownership was 8.0 in lymphoma households compared to 4.1 yr in controls. This excess was probably due to an increase in the number of yr during which cats were kept in lymphoma households rather than to a greater number of lymphoma households with cats. This apparent excess of lymphoma cases in catkeeping households was accounted for by failure to match controls with index households for duration of residence at the same address. No difference was found between index and control households in the numbers of yr that cats had been owned, the number of index and control households with cats, the average number of cats owned, and the percentage of male cats (which are more susceptible to feline lymphoma) were not of statistical significance for incidence of cancer. Nor was there any strong evidence for a correlation between cause of cat death (e.g. malignancy, cardiac trouble) and incidence of cancer in owners' households. No differences were found between control and index households in the patterns of ownership of dogs or parakeets. Furthermore, 70-80% of family members with cancer did not own cats, which makes it seem unlikely that a causal connection exists between cat ownership and human malignant disease.

1183 THE ENVIRONMENTAL DISTRIBUTION OF CANINE RESPIRATORY TRACT NEOPLASMS. (E.) Reif,

J. S. (Sch. Vetr. Med., U. Pennsylvania, Philadelphia) and D. Cohen. *Arch Environ Hlth* 22(1):136-140, 1970.

The possibility of a relationship between canine respiratory tract neoplasia and residence in an urban environment involving exposure to polluted air was explored. Case records of all dogs with histologically proven primary neoplasia of the lungs and bronchi, nasal passages and paranasal sinuses, tonsils, stomach and intestine seen in a veterinary hospital from 1952-1969 were reviewed. The case material included 51 dogs with lung and bronchial carcinoma, 57 with carcinoma of the nasal passages and paranasal sinuses, and 57 with carcinoma of the tonsils. A group of 74 dogs with neoplasms of the stomach and intestine served as controls. The mean ages for dogs with neoplasms of the 4 sites studied showed clustering around the age of 10.5 yr. Forty-seven percent of cases of carcinoma of the lungs and bronchi, and a similar proportion of cases of carcinoma of the nasal passages and paranasal sinuses were composed of dogs from urban environments. However, 73.7% of cases of carcinoma of the tonsils were composed of dogs from urban environments. Sixty percent of all dogs

re from urban environments, and 47% of dogs with gastrointestinal carcinomas were from urban environments. Most of the dogs with carcinoma of the asils were mongrels, possibly reflecting the relative rarity of purebred dogs residing in urban environments.

34 EPIDEMIOLOGY, CLINICAL AND RADIOLOGICAL FEATURES OF PRIMARY LUNG CANCER. A REPORT ON 120 CASES DETECTED AT THE ANTITUBERCULOSIS CONSORTIUM IN ALESSANDRIA. (It.) Calamari, F. (Provincial Antituberculosis Consortium Alessandria, Italy) and L. Prigione. *Riv Ist Vaccinogeno* 20(3): 3-24, 1970.

The detection of 120 cases of primary lung cancer during the yr 1968-1969 in the district of Alessandria (southern Italy) revealed an incidence of 4 per 100,000 inhabitants and an index of 24.7 per 100,000 inhabitants within the population above yr-of-age. When focused on the male population between 35 and 64 yr-of-age, this index increased to 59.9 per 100,000 inhabitants. The incidence of primary lung cancer in the urban area of Alessandria appeared to be higher than in any other part of Italy, probably due to its chromate manufacturing industries; this index appeared very high within the towns of Acqui Terme and Ovada with a prevalent agricultural economy but with a large part of its population involved in the industry of Alessandria. The contribution of air pollution, occupational exposure (chromium, asbestos, Ni, As, iron des and radioactive metals) and cigarette smoking to the increase of lung cancer incidence is re-evaluated.

5 SOME STATISTICAL DATA ON THE CARCINOGENIC HAZARDS FOR WORKERS INVOLVED IN THE PRODUCTION OF NICKEL FROM OXIDIZED ORES. (Rus.) Shabynina, A. V. (Inst. Work Hyg. and Occupational Health, Sverdlovsk, USSR) and N. K. Shabynina. *Gig Prof Zabol* 14(11):10-13, 1970.

The incidence of cancer among workers from a nickel concentration and melting plant in the Urals was compared to that of the city population. Data were obtained from records covering the period from 1955-1967. Mortality from lung cancer was 2.8 times higher among nickel workers than among the urban population; lung cancer among the plant workers was limited only to males above the age of 40 yr, who spent an average of 13 yr at this activity. Within the plant the highest cancer incidence, 2.1 times the cancer incidence among the urban population, was found in the roaster section (reduction of nickel) due to exposure to nickel sulfide and nickel oxide-containing dusts and in the cobalt section due to cobalt and arsenic exposure (1.4 times the urban population). The incidence of mesosarcoma among workers of the 40-50 yr group was 6.2 times that of the city population.

1186 FATAL TESTIS TUMORS IN THE FEDERAL REPUBLIC ARMY. (Ger.) Altwein, J. E. (U. B. Mairrose and K. Wegner. Mainz, Germany) *Med Monatsschr* 24(11):489-493, 1970.

An evaluation of the mortality rate among the soldiers of the Federal Republic due to testicular tumors is presented. Out of 70 soldiers in whom such tumors were discovered between 1956 and 1969, 66 were diagnosed as such. The tumors were classified under the headings of: seminoma (SE), embryonal carcinoma (EC), and teratocarcinoma (TC). The distribution of the 66 cases was: 39 with TC, 17 with SE, and 5 with EC. The remaining 5 cases appeared to have a retroperitoneal tumor with clinically inconspicuous testicular involvement which was proven histologically. The total mortality rate for testicular tumors amounted to 1.6/100,000 soldiers. The peak for the age distribution of death from this cause was 21 years. No familial connection was revealed in the incidence of this disease, and the case histories did not reveal any early virus infection such as mumps as a causal effect.

1187 AGE AT FIRST BIRTH AND BREAST CANCER RISK. (E.) MacMahon, B. (Dept. Epid., Harvard Sch. Pub. Hlth., Boston), P. Cole, C. R. Lowe, A. P. Mirra, B. Ravhihar, E. J. Salber, V. G. Valaoras, and S. Yuasa. *Bull WHO* 43(2):209-221, 1970.

The association between age, parity, and risk of developing breast cancer was investigated in a global study of more than 4000 cases of breast cancer. Study populations were examined in 7 test centers: Boston, Glamorgan (Wales), Athens, Slovenia (Yugoslavia), Sao Paulo, Taipei, and Tokyo. Estimated breast cancer risks for women of parity 5 or more were from 40-60% of risks for the nulliparous. In all 7 centers, risk of developing breast cancer increased with the age at which a woman had her first child; women having the first child under the age of 20 yr had only 33% of the risk of women having their first child at age 35 yr or more. Risks for women having their first child at from 30-34 yr of age were similar to risks for nonparous women. Generally, risk of breast cancer increased linearly with increasing age at first birth till 30 yr; for women having their births when under 20 yr old, the risk of breast cancer decreased as age at first birth decreased. The association of breast cancer risk with age at first birth was not a simple reflection of the low parity of breast cancer patients. Births after the first had relatively little effect on breast cancer risk.

1188 NEOPLASMS OF CHILDHOOD AFFECTING THE HEAD AND NECK. (E.) Smoler, J. (Nat'l. Med. Ctr., I.M.S.S., Mexico City, Mexico), G. Velazquez, G. Vivar and S. Levy-Pinto. *Oto-Rhino-Laryngology* 206:863-866, 1970.

The incidence, pathology, and clinical course of neoplasms of the head and neck affecting children were reviewed. Prominent among these tumors is Burkitt's lymphoma, a malignant neoplasm of primarily undifferentiated lymphoreticular cells. Burkitt's lymphoma in African cases often appears as a jaw tumor, while abdominal tumors are also seen. The mean age of 21 patients with Burkitt's lymphoma was 10.6 in 1 study. Twelve of 18 American Burkitt patients presented bone marrow involvement, while only 2 of 33 African patients showed marrow involvement. A herpes-like virus has been found in 100% of clinically proven African Burkitt's lymphoma cases in 1 study. Benign tumors of the head and neck observed in a pediatric hospital (149 total cases) included 39 hemangiomas, 36 papillomas, 26 lymphangiomas, 17 ranula, and 10 juvenile angiofibromas. All benign tumors were treated with surgery with good results. Of 78 malignant head and neck tumors observed at the same children's hospital, 30 were reticuloendothelioses, 18 were Hodgkin's disease, 8 were lymphoblastic lymphoma, 5 were reticulosarcoma, and 4 were rhabdomyosarcoma. All cases of metastasizing malignancies which were treated with radiotherapy and/or chemotherapy proved fatal.

- 1189 BACTERIA AND AETIOLOGY OF CANCER OF THE LARGE BOWEL. (E.) Hill, M. J. (St. Mary's Hosp. Med. Sch., London, England), B. S. Drasar, V. Aries, J. S. Crowther, G. Hawksworth and R. E. O. Williams. *Lancet* 1(7690):95-100, 1971.

The association between high incidences of carcinoma of the colon and fecal bacteria and steroid content was investigated. Feces from subjects in 6 countries were examined for the presence of bacterial flora and steroids; the populations studied were from England, Scotland, the United States, India, Uganda, and Japan. Feces from Britain and the United States, where the incidence of colon cancer is high, had larger amounts of *Bacteroides* and smaller amounts of enterococci than feces from India, Uganda, or Japan. Mean \log_{10} colonies/g wet wt of fecal matter from the British Isles and United States were 9.7-9.8 for *Bacteroides* spp., while counts for this bacterium from Uganda and India were 8.2 and 9.2, resp. Mean \log_{10} colonies/g wet wt for enterococci for fecal samples from Uganda, India, and Japan ranged from 8.2-9.4, while counts for enterococci from England, Scotland and the United States ranged from 5.0-5.9. Feces from peoples in Western countries contained higher concentrations of steroids than those from African and Eastern countries, and the steroids were more degraded in the former groups. The results are consistent with the hypothesis that the intestinal bacteria may be related to cancer of the colon.

- 1190 CANCER IN MALMÖ 1958-1966. (Nor.) Berge, T. (Inst. Pathol. Malmö, Norway) and S. Lundberg. *Läkartidningen* 67(47):5531-5536, 1970.

- 1191 THE SIMULATED POPULATION METHOD OF ANALYSIS OF ANIMAL PAINTING EXPERIMENTS IN CANCER RESEARCH. (E.) Lee, P. N. (Tobacco Res. Council La Harrogate, Yorkshire, England). *Biometrics* 26(4):777-785, 1970.

- 1192 EPIDEMIOLOGICAL EVALUATION OF INCIDENCE AND MORTALITY DUE TO PULMONARY CARCINOMA IN THE POPULATION OF THE CITY OF WARSAW IN THE YEARS 1963-1967. (Pol.) Koszarowski, T. (Inst. Oncol. Warsaw, Poland), H. Gadomska and Z. Karewicz. *Pol Arch Med Wewn* 45(3):451-459, 1970.

- 1193 THE NATIONAL CANCER RECORD. (Sp.) Baraja, E. (Nat'l. Inst. Cancer, Mexico). *Salud Publ Mexico* 12(4):463-466, 1970.

- 1194 THE CANCER RECORD IN MEXICO. (Sp.) Baraja, E. (Nat'l. Inst. Cancer, Mexico). *Rev In Nac Cancer* 22:681-683, 1970.

- 1195 CANCER IN MEXICO. STATISTICS. CAMPAIGN (Sp.) Zuckermann, C. (Nat'l. Cancer Inst Mexico). *Acta Oncol* 9(1):48-55, 1970.

See also:

- * (Rev): 0847, 0857, 0858, 0868, 0873
- * (Viral): 1082
- * (Path): 1157
- * (Misc): 1248

- 196 ENZYMATIC ACTIVITIES OF TUMORS OF THE NERVOUS SYSTEM *IN VIVO* AND *IN VITRO*. (E.) Brunner, M. L. (U. Utah Coll. Med., Salt Lake City). *Arch Path* 91(2):148-155, 1971.
- Istochemical differences in nicotinamide adenine dinucleotide tetrazolium reductase (NADH reductase), lactate dehydrogenase (LDH), glucose-6-phosphate dehydrogenase (G6PDH) and acid phosphatases between sections of nervous system tumors (astrocytoma, glioblastoma, ependymoma, meningioma and schwannoma) and cells of the same tumors grown *in vitro* were investigated by appropriate staining methods. In general, the enzymes studied underwent a transient decrease in activity during the first week of *in vitro* growth, but then returned to the same levels as in the parent tumor. LDH activity stabilized at 80% of the levels found in the parent tumor in glioblastoma cultures and at 50% of the parent tumor levels in choroid plexus papilloma cultures. G6PDH activity increased almost 2-fold in glioblastoma cultures and 5-fold in schwannoma cultures compared to the parent tumors. Most cultures showed some mesenchymal activity. With all cultures developed moderate numbers of large, bizarrely-shaped, multinucleated cells lying about the periphery of outgrowth; these cells showed faint NADH reductase, LDH, G6PDH and acid phosphatase activities.
- 97 LYMPHOCYTE SENSITISATION: AN *IN VITRO* TEST FOR CANCER? (E.) Field, E. J. (Newcastle Gen. Hosp., England) and E. A. Caspary. *Lancet* 7687):1337-1341, 1970.
- Sensitization of blood lymphocytes from patients with malignant disease to a basic protein, encephalogenetic factor (EF) and to a basic protein derived from the human sciatic nerve (SNBP) was observed. The presence of these proteins as antigens, guinea pig macrophages migrate more slowly in cultures of sensitized human lymphocytes. Tests for lymphocyte sensitization were performed on 38 healthy subjects and on 56 patients with malignancies including carcinoma of the cervix, bronchus, kidney, breast and bladder. Among the controls, macrophage migration was inhibited by 0.9-3.6%. All 56 cancer patients, with or without signs of non-metastatic nervous involvement, showed marked inhibition of macrophage migration with EF (8.2-29.9%) and SNBP (7.7-30.4%). Patients harboring an untreated carcinoma did not react differently from patients who had undergone successful cancer therapy. The type of neoplasm did not affect the reactions. Tests on patients with benign neoplasms showed normal values for the sensitivity to the protein antigens.
- 98 INFLUENCE OF THE LETHAL YELLOW (AY) GENE ON DEVELOPMENT OF RETICULAR NEOPLASMS. (E.) Dinger, M. K. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *J Nat Cancer Inst* 45(6):1205-1210, 1970.
- The influence of the lethal yellow gene (AY) on the development of reticular tumors was investigated. A strain of "yellow" mice, (YBR x AKR)_{F1} hybrids, was

developed in which the presence of the gene increased susceptibility to spontaneous reticular neoplasms. Mice having the (AYa) gene developed reticular tumors at earlier ages (21-22 months) than did mice having the (aa) gene (26-28 months). The lethal yellow gene also appeared to increase susceptibility to spontaneous hepatomas (97-100% vs 51-63%) and to spontaneous pulmonary tumors (at 20-22 months vs 27-30 months). The "yellow" hybrid mice also developed unusual liver tumors, interstitial cell tumors in the testis of males, and thymic lesions. "Yellow" hybrids showed increased body size compared to mice not bearing the AY gene; differences of 18 g at 6 and 12 months of age between males carrying the AYa and aa genes were recorded, and differences of 24 and 22 g at 6 and 12 months of age were recorded for females with and without the lethal yellow gene.

- 1199 POSTCASTRATIONAL ADRENAL TUMORS IN TWO STRAINS OF MICE: MORPHOLOGIC, HISTOCHEMICAL, AND CHROMATOGRAPHIC STUDIES. (E.) Krishna Murthy, A. S. (Child. Hosp. Med. Ctr., Boston, Mass.), M. A. Brezak and A. G. Baez. *J Nat Cancer Inst* 45(6):1211-1222, 1970.

Adrenal tumors which developed in strain DBA and strain CE mice of both sexes following castration were compared morphologically. DBA mice were examined on autopsy 6 and 12 months after castration, while CE mice were examined 12 months after castration. DBA adrenal tumors showed nodular hyperplasias and adenomas with low levels of succinate dehydrogenase activity and high levels of 3 β -hydroxysteroid dehydrogenase activity. The DBA tumors contained estrone, and uteri were progressively stimulated. Adrenal cortical tumors developed by CE mice were larger than those developed by DBA mice; tumors in CE mice also more pleomorphic histologically. CE tumors showed intense succinate dehydrogenase activity and variable 3 β -hydroxysteroid dehydrogenase activity. Estrone was also present in extracts from CE tumors, and uteri were stimulated. In both strains of mouse, pituitary gonadotropins were increased at 6 and 12 months. Androgen was evidently not produced in the seminal vesicles of either strain.

- 1200 COMPARISON OF METHYL-LABELED tRNA IN A NEOPLASTIC CELL LINE WITH A PAIRED NON-NEOPLASTIC CONTROL. (E.) Quinn, C. E. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), R. Gantt and V. J. Evans. *Exp Molec Path* 13(2):231-241, 1970.

Methylation of tRNA was compared in intact cells from a non-neoplastic mouse embryo cell line grown in NCTC 135 medium supplemented with 10% fetal calf serum and a neoplastic cell line derived from the non-neoplastic cell line by changing the medium to one with 10% horse serum. By growing the non-neoplastic mouse cell line in ³H-methylmethionine and the neoplastic line in ¹⁴C-methylmethionine, it was possible to simultaneously extract, isolate and chromatograph the tRNA from the 2 different systems. Comparison of reversed-phase chromatography profiles of methylated tRNA indicated a small chromatographic heterogeneity, but the differences appeared to be quantitative rather than qualitative. Because of the minimal differences

in the experimental system of the two cell lines (the neoplastic line being derived from the non-neoplastic one) and the simultaneous isolation of tRNA, the differences in methylation appear to be real and may bear some relationship to malignancy.

- 1201 LEUKAEMIC TRANSFORMATION OF ENGRAFTED HUMAN MARROW CELLS *IN VIVO*. (E.) Fialkow, P. J. (Dept. Med. Genet., U. Washington, Seattle), E. D. Thomas, J. I. Bryant and P. E. Neiman. *Lancet* 1(7693):251-255, 1970.

A case is reported of a 16-yr-old girl with acute lymphoblastic leukemia in whom there was a leukemic transformation of engrafted marrow cells donated by her brother. The patient was given a 1000 rads midline tissue dose of whole-body irradiation on the day before she was given 14×10^9 nucleated marrow cells from her HL-A matched sib. Two wk later, the patient's white blood cell count reached a minimum of 20 cells/mm³, thereafter rising to 1500 cells/mm³ on day 19. Apparently, the marrow cell graft had been successful, and only donor-type XY cells were found in uncultured marrow from the patient. Sixty-two days after the marrow graft, the patient's leukemia recurred, and cytogenetic studies showed that the leukemia had affected the previously normal XY graft cells. It was suggested that the transformation of the normal XY cells was caused by the activation of a leukemogenic agent, possibly viral, in the susceptible cells. Alternatively, such an agent may have been transferred to the donor cells from the leukemic cells of the recipient.

- 1202 STUDIES OF DNA-INDUCED HERITABLE ALTERATION OF MAMMALIAN CELLS. (E.) Borenfreund, E. (Sloan-Kettering Inst. Cancer Res., New York, N. Y.), Y. Honda, M. Steinglass and A. Bendich. *J Exp Med* 132(6):1071-1089, 1970.

Normal Chinese hamster cells (CH) were exposed to mouse Ehrlich ascites tumor cells (EA) to study the interactions resulting from co-culture. Several hr after co-culture was begun, adhesions and bridges between the 2 cell types were seen. When immunofluorescent techniques were applied to co-cultures of CH and EA, the intercellular connections were seen to contain mouse antigen but not CH antigen. An occasional transfer of ³H-thymidine-labeled DNA from EA to CH was observed by radioautographs. After 10 wk of subculturing, a new cell type with the atypical immunofluorescence reaction of control preparations of EA was observed. Karyotype analysis revealed 22 or 23 CH chromosomes in these cells; the subcultures were stable for 1 yr. Some of the clones induced transplantable tumors in the cheek pouches of cortisone-treated weanling Syrian hamsters. Incubation of CH with EA-DNA resulted in the acquisition of the same antigenic properties as EA by the CH.

- 1203 MESSENGER RNA IN HeLa CELLS: AN INVESTIGATION OF FREE AND POLYRIBOSOME-BOUND CYTOPLASMIC MESSENGER RIBONUCLEOPROTEIN PARTICLES BY KINETIC LABELLING AND ELECTRON MICROSCOPY. (E.)

Spohr, G. (Swiss Inst. Res. Exp. Cancer, Lausanne), N. Granboulan, C. Morel and K. Scherrer. *Europ J Biochem* 17(2):296-318, 1970.

Ribosomal RNA synthesis in HeLa cells was inhibited (actinomycin D, 0.05 µg/ml), and cytoplasmic messenger RNA (mRNA) and messenger-like (mlRNA) were investigated. Non-ribosomal RNA (6-7 S) of the cytoplasm existed in the form of ribonucleoprotein complexes pre-existing in the cell and were stable to cell lysis and isolation procedures. mRNA was contained in a mRNA-protein complex associated with ribosomes (density 1.6) and was released by EDTA treatment (density 1.40-1.48). The free mlRNA of the cytoplasm and the mlRNA-protein particles showed the same sedimentation characteristics as mRNA. The kinetics of synthesis and decay of ribonucleoprotein complexes of mlRNA and polyribosome-bound mRNA were followed by labeled uridine incorporation. After 30 min of incubation, free mlRNA-protein was labeled almost exclusively; subsequently, polyribosome-bound label appeared and after 4 hr both mRNA-protein and free mlRNA-protein were equally labeled. Decay was monitored by adding 5 µg actinomycin D to incubation mixtures after 6 hr of labeling; the same rate of decay was observed in both fractions, indicating that the mlRNA in free particles did not represent a precursor of polysome-bound mRNA, or the high dose of actinomycin D may have inhibited any equilibrium which exists between the 2 RNAs. Electron microscopy revealed small, rounded, cytoplasmic particles ranging 100-200 Å in diameter, which may correspond to the mRNA-protein complex.

- 1204 UPTAKE OF TRANSFER RIBONUCLEIC ACID BY NORMAL AND LEUKEMIC CELLS. (E.) Herrera, F. (Natl. Cancer Ctr., Natl. Inst. Hlth., Bethesda, Md.), R. H. Adamson and R. C. Gallo. *Proc Nat Acad Sci* 67(4):1943-1950, 1970.

Uptake of tRNA into mammalian cells was demonstrated in the murine leukemia, L1210, and in a human lymphoblast (NC037) cell lines. The rate of uptake of tRNA in fresh, human lymphocytes was extremely rapid with uptake being proportional to tRNA concentration up to 50 µg/ml, and plateau levels were reached by 500 µg/ml. Similar kinetics of tRNA uptake were noted in murine leukemia cell line. The percentage of L1210 cells stained with nigrosine dye was 2% in both untreated cells and cells incubated with *E. coli* tRNA. Median survival time of mice inoculated with control and tRNA-treated L1210 leukemic cells did not differ. Thirty to 70% of cells incubated with ¹⁴C-tRNA were labeled during 2 min of incubation, which resulted in vesicle formation characteristic of pinocytosis; radioactivity was present in all subcellular fractions after 5 min of incubation with the nucleus containing 25-60% of the counts. *E coli* tRNA recovered from L1210 cells accepted leucine and could still be methylated, indicating that mammalian cells can take up exogenous tRNA and that an appreciable percentage may remain functional for at least 1 hr. It is possible that tRNA may exert regulatory functions in cell differentiation which may be clarified by experiments based on a nonphysiological input of foreign tRNA.

- 1205 ESTROGEN-INDUCED VARIATION OF LYSINE TRANSFER RIBONUCLEIC ACID ISOACCEPTORS IN CHICKEN LIVER. (E.) Busby, W. F., Jr. (Worcester Found. Exp. Biol., Shrewsbury, Mass.) and P. Hele. *Biochem Biophys Acta* 224(2):413-422, 1970.

The effect of diethylstilbestrol on lysyl-transfer RNA isoacceptors was studied in chicken liver. Young (10-14 wk) chickens were given i.m. injections of diethylstilbestrol (5 mg/100 g body wt) and lysyl-transfer RNA was assayed in the liver by a pH5 precipitation procedure. Prior to treatment with diethylstilbestrol, it was found that transfer RNA produced by laying hens' livers contained 25% more lysyl-transfer RNA than did RNA produced by the livers of cocks or immature hens. The amount of lysyl-transfer RNA in livers of immature birds was 1.49-1.76 nmoles/mg transfer RNA, while the amount of lysyl-transfer RNA in the livers of laying hens was 2.03-2.08 nmoles/mg transfer RNA. Formation of lysyl-transfer RNA in time was higher in diethylstilbestrol-treated birds than in controls; after 5 min of incubation, livers of treated birds produced 48 pmoles of ^{14}C -labeled lysyl-transfer RNA/assay, while controls produced 40 pmoles of lysyl-transfer RNA in the same time. Sixty-five hr after treatment with diethylstilbestrol, lysyl-transfer RNA of treated birds was increased by about 25% over that of controls; the increase was independent of the sex of the bird. Increased lysyl-transfer RNA was recorded for treated birds whether the synthetase preparation was made from control or from diethylstilbestrol-treated chickens. In transfer RNA preparations from diethylstilbestrol-treated chickens, an 18.7% increase in seryl-transfer RNA, and a 9.4% increase in arginyl-transfer RNA were noted. Two species of lysyl-transfer RNA were discovered in control and diethylstilbestrol-treated birds on co-chromatography on methylated albumin-kieselguhr columns. Treated chicken livers contained a marked increase in 1 of these species of lysyl-transfer RNA relative to the other species.

- 1206 THE SÉZARY SYNDROME. CYTOGENETIC STUDIES AND IDENTIFICATION OF THE SÉZARY CELL AS AN ABNORMAL LYMPHOCYTE. (E.) Crossen, P. E. (Dept. Med. Res., Kanematsu Mem. Inst., Sydney Hosp., Australia), J. E. Mellor, A. G. Finley, R. B. M. Ravich, P. C. Vincent and F. W. Gunz. *Amer J Med* 50(1):24-34, 1970.

A case of Sézary syndrome exhibited abnormal leukocytes in the blood over 4 yr of observation. The patient was a 56-yr-old woman who presented with an indolent, intensely pruritic erythroderma accompanied by local scaling of the skin and loss of body hair. Her blood contained moderate numbers of atypical lymphoid cells (2000-5000 cells/mm³) characteristic of the Sézary syndrome. The skin lesions were thought to be prelymphomatous in character, but no systemic changes of lymphoma developed. Cultures of leukocytes were incubated with phytohemagglutinin (PHA), whereupon they demonstrated highly active RNA and DNA synthesis and subsequent cell division. Three cell lines were discovered, with modes of 76, 46, and 98-100 chromosomes. In PHA-

stimulated cultures, the 7-76 chromosome cells were most common, accounting for 10 and 32 cell types, resp., as opposed to 1-7 cells having other chromosome numbers. The abnormal Sézary cells were thought to belong to the lymphoid series and to be potentially neoplastic. The Sézary syndrome was thought to be transformed to a true lymphoma condition upon breakdown of control mechanisms regulating lymphocyte numbers.

- 1207 SUPPRESSION OF MAMMARY HYPERPLASTIC NODULE FORMATION AND PITUITARY PROLACTIN SECRETION IN MICE INDUCED BY ERGOCORNINE OR 2-BROMO- α -ERGOCRYPTINE. (E.) Yanai, R. (Natl. Cancer Ctr. Res. Inst., Tokyo, Japan) and H. Nagasawa. *J Nat Cancer Inst* 45(6):1105-1112, 1970.

The effect of treatment with ergocornine or with 2-bromo- α -ergocryptine (CB-154) on the development of mammary hyperplastic nodules and on pituitary prolactin secretion was investigated in female mice. Mice were given daily s.c. injections of 0.2 mg ergocornine methanesulfonate or 0.2 mg CB-154 for 20-23 days or for 40-43 days. The wt of the anterior pituitary and the ovarian wt were significantly decreased in mice given CB-154 and in those given ergocornine for both dose periods. Mice given CB-154 for 20 days developed 23% as many nodules as controls; mice given ergocornine for 29 days developed 39% fewer nodules than controls. Mice treated for 40 days with ergocornine had only 20% of the number of nodules developed by controls, and mice given CB-154 for 40 days developed 8% as many nodules as controls. The average size of nodules in mice given CB-154 was 0.45 mm, while the average size of nodules in controls was 0.67 mm; mice given ergocornine developed nodules which averaged 0.49 mm in size. Numbers of regressed nodules were greater in treated animals than in controls for both dose periods, with ergocornine-treated mice showing 3.6 regressed nodules at 40 days, and CB-154-treated mice showing 2.0 regressed nodules, compared to 0.5 regressed nodules in controls. Lobuloalveolar development was limited in the mammary glands of treated animals, while controls showed moderately developed lobuloalveolar systems. Anterior pituitary prolactin secretion was decreased by the ergot alkaloids to 54-60% of control values, with decreases being more pronounced in the 40-day treatment group.

- 1208 EPIDERMAL CHALONE AND CELL PROLIFERATION IN A TRANSPLANTABLE SQUAMOUS CELL CARCINOMA IN HAMSTERS: II. *IN VITRO* RESULTS. (E.) Laurence, K. R. (Mitosis Res. Lab., Birkbeck Coll., U. London, England) and K. Elgjo. *Virchow Arch Zellpath* 7(1):8-15, 1971.

Extracts of a keratinizing transplantable hamster tumor were tested for their content of epidermal chalone, using normal mouse ear cultures with Colcemid as a test system. A 67% depression of the mitotic rate of mouse ear epidermis was found with tumor extract compared to controls; a 45% depression in mitosis was observed with epidermal chalone from pig skin. The pig skin preparation also inhibited mito-

sis in mouse ear sebaceous glands, but extracts of hamster tumor did not. The mitotic rate of tumor tissue itself was not affected by skin or liver extracts with or without the addition of adrenalin and hydrocortisone. Possible reasons for the lack of response of the hamster epithelial tumor to epidermal chalone *in vitro* may be altered permeability characteristics of the tumor cell, or it may be that this tumor is well-differentiated and the growth fraction so small that changes were not detectable by the methods used.

- 1209 AN ELECTRON MICROSCOPIC STUDY OF METAPLASIA OF THE RAT TRACHEAL EPITHELIUM IN VITAMIN A DEFICIENCY. (E.) Wong, Y. C. (Fac. Med. U. Western Ontario, London, Canada) and R. C. Buck. *Lab Invest* 24(1):55-66, 1971.

The morphological development of metaplasia of the tracheal epithelium of rats fed a vitamin A-deficient diet was followed over a 22 wk period by electron microscopy. Differentiated ciliated and goblet cells decreased in number and lost the highly specific features found in normal cells (cilia, mucus granules, and microvilli). Hyperplastic nests of basal cells appeared to be the first evidence of metaplasia, and these clusters spread with desquamation of the surface epithelium. The hyperplastic cells differentiated into flatter cuboidal cells near the surface (squamous cells) which progressively showed an increase in desmosomes, keratohyaline granules, keratin filaments, and membrane-coating granules. The boundary between nonmetaplastic and metaplastic epithelium was abrupt with desmosomes between the 2 types of epithelium. Metaplastic transformation of the epithelium apparently does not involve differentiated cells but is a result of differentiation of the generative cell in a new direction.

- 1210 REVERSAL OF MALIGNANT TRANSFORMATION BY TUMOR DNA. (E.) Halpern, B. C. (Dept. Chem, U. California, Los Angeles), R. M. Halpern, S. Q. Chaney and R. A. Smith. *Proc Nat Acad Sci* 67(4):1827-1833, 1970.

The *in vivo* infectivity of Walker-256 carcinosarcomas cultured with DNA prepared from the same tumor was investigated. Growth in tissue culture medium of Walker carcinosarcomas with tumor cell DNA did not affect the *in vitro* growth of tumors. However, tumor cells cultured with DNA exhibited a reduced capacity to induce malignant tumors when injected into rats. Female rats were given s.c. injections of 10^5 tumor cells grown in culture with tumor cell DNA; controls were injected with tumor cells of the same type which had not been treated with DNA. Thirty days after injection, 3 of 10 rats given tumor cells grown with DNA for 48 hr were dead with neoplasms, while 8 of 10 rats given untreated tumor cells were dead with tumors. At 30 days, 7/10 of the rats injected with untreated cells cultured for 72 hr had developed tumors, while only 1 of 10 rats given cells cultured with DNA for 72 hr had developed neoplasms. Coincident with the reduced virulence of DNA-treated tumor cells was a decrease in

transfer RNA methylase activity in DNA-treated cells. After a 48-hr exposure to DNA, cells showed a specific transfer RNA methylase activity of 179 pmoles of ^{14}C incorporated/mg protein in 45 min, while untreated cells showed a specific transfer RNA methylase activity of 365. When DNA was removed from the growth medium, the virulence of cells was fully restored, and the inhibition of transfer RNA methylase disappeared.

- 1211 VILLOUS TUMOURS OF THE RECTUM ASSOCIATED WITH SEVERE FLUID AND ELECTROLYTE DISTURBANCE. (E.) Lee, R. O. (Northampton Gen. Hosp., England) and D. Keown. *Brit J Surg* 57(3):197-201, 1970.

Electrolyte disturbance leading to renal failure and associated with villous tumors of the rectum is described in 2 case reports, a female aged 74 yr and a male aged 77 yr. Comparison of the concentrations of sodium and potassium in the blood and rectal fluid from the 2 patients showed that, while sodium levels were similar in the 2 cases, potassium concentrations were 10-20 times higher in one case than in the other. The ratio of sodium to potassium lost in rectal fluid in the 2 cases was 3-4 : 1. It appeared that electrolyte loss associated with the adenomas was general and not limited to loss of potassium.

- 1212 NATURAL EVOLUTION AND PATHOLOGICAL ALTERATIONS OF LYMPHOID CELL PROTEINS: ELECTROPHORETIC PATTERNS OF SOLUBLE AND INSOLUBLE COMPONENTS. (E.) Mobarak, M. A. (U. Pennsylvania Sch. Med., Philadelphia) and J. I. Brody. *Clin Chim Acta* 30(3):635-643, 1970.

The electrophoretic patterns of cellular proteins of various lymphoid organs were investigated, and compared with those of lymphocytes from a patient with chronic lymphocytic leukemia. Four prealbumins were detected in agar gel electrophoresis of normal human lymph node cell extract; most proteins were located in the γ -globulin electrophoretic zone. In lymphocytes from the patient with chronic lymphocytic leukemia, the fastest prealbumin band had 2 anodic branches which gave this zone a semilunar appearance. Most of the protein was located at a peak of m_r 1.43 and appeared as a dense, broad, ill-defined band with striated and unequal vertical margins, the anodal being shorter than the cathodal border. The γ -globulin region was diffuse with ill-defined margins. No differences were noted between the electrophoretic appearances of normal thymus from subjects aged from neonate to 6 months, pre- and post-adolescent normal tonsil, and pre- and post-senescent normal lymph node extracts. When electrophoretic studies were performed on water-insoluble lymphocyte proteins, using urea/formate starch gel, it was found that thymus extracts from subjects of age range 6-24 months showed the smallest number of bands with electrophoretic mobilities comparable to those of serum albumin. Benign thymoma showed an electrophoretic pattern similar to that of normal thymus from infants aged 2-6 months. Giant follicular lymphoma showed a

faint fast-moving band. Extracts from chronic lymphocytic leukemia and from Hodgkin's paraganuloma lymph nodes were similar, with broad ill-defined bands covering both the albumin and prealbumin areas. The major protein component of residues from patients with lymphocytic lymphoma was a broad, ill-defined band adjacent to the cathodal margin of the application slot, in addition to 3 narrow bands in the prealbumin region.

1213 CLINICAL AND PATHOLOGICAL CORRELATION OF NONPIGMENTED TUMORS OF THE CONJUNCTIVA AND PINGUECULAS AMONG AFRICANS. (E.) Ticho, U. (Hadassah Med. Ctr., Jerusalem, Israel) and I. Ben-Sira. *Amer J Ophthalmol* 70(5):757-763, 1970.

The histopathological appearance of nonpigmented tumors of the conjunctiva was observed in 103 African patients. The case material comprised 80 males and 23 females presenting with 1 of 3 types of lesion: pingueculas, elevated glistening white lesions surrounded by pigment, and fleshy protruding lesions of an invasive nature. The pingueculas (25 patients) presented a localized whitish-yellow swelling without keratin covering and with deeply placed blood vessels. Only stromal changes were manifested histologically, consisting of degeneration of the elastic fibers and hyalinization of the connective tissues. The elevated glistening lesions (70 cases) appeared to have originated from pingueculas, the glistening aspect was due to a keratin covering of the lesion. Deeply placed blood vessels were present. The epithelium showed various stages of dyskeratosis, ranging from simple epidermalization to intraepithelial cancer *in situ*. The stroma in this group were not invaded, but showed hyaline and elastic degenerative changes marking pinguecula. Fleshy protruding lesions (8 cases) were papillomatous to cauliflower in shape. Tumors invaded the cornea or sclera. Histopathologically, these lesions showed squamous cell carcinoma with invasion; in 5 cases, epidermalization and other dyskeratotic changes characteristic of other lesion types were seen.

1214 FACTORS CONTROLLING THE GROWTH OF THE YOSHIDA ASCITES TUMOR IN THE UTERUS OF THE RAT. (E.) Lions, J. (Dept. Vetr. Clin. Stud., U. Cambridge, England). *Brit J Exp Path* 51(5):453-463, 1970.

The effect of hormonal status on the growth of transplanted Yoshida ascites sarcomas in the uterus of rats was investigated. Female rats were divided into experimental groups, including intact rats with normal estrous cycles, ovariectomized rats, pseudopregnant rats, rats given injections of 0.2 µg estradiol-17β/day, and rats given estradiol and 2 mg of progesterone/day. Rats were given i.p. injections from a Yoshida ascites sarcoma. No tumor growth was observed in intact rats with normal estrous cycles; dead sarcoma cells were found in the uterine lumen in 3 rats. Four of 8 ovariectomized rats showed tumor growth in the uterus. Three of 6 ovariectomized rats given estrogen showed tumor growth; 3 of 6 ovariectomized rats given estrogen and progesterone showed tumor growth. Five of 6

ovariectomized rats given progesterone without other treatment showed tumor growth, and all 7 ovariectomized rats given progesterone and a single dose of estrogen developed tumors. Twenty of 23 intact rats in the 4th day of pseudopregnancy developed tumors, and 7 of 8 rats in the 5th day of pseudopregnancy developed tumors. Scratching the endometrium, and inoculating sarcoma cells directly into the endometrial stroma, permitted tumor growth in the uterus of rats with normal estrous cycles, a finding which may suggest that the uterine epithelium is important for resistance of the uterus to tumor development.

1215 MAMMARY TUMOR DEVELOPMENT IN BR6 MICE: HORMONAL STIMULATION. (E.) Lee, A. E. (Imperial Cancer Res. Fund, London, England). *Brit J Cancer* 24(3):568-573, 1970.

The effect of hormone injections and pituitary implantation on the growth of mammary tumors was investigated in mice. Hormone injections consisted in 1.0 mg prolactin, 0.5 I.U. adrenocorticotrophic hormone, 50.0 µg growth hormone, 0.5 µg estrone and 0.5 mg progesterone; in some cases, hormone injections were accompanied by injections of 5-hydroxytryptamine (5-HT). When breeding females with regressed pregnancy-dependent mammary tumors were given hormone injections, 3 of the 6 treated mice showed recurrence of tumor growth after 1 course of treatment; 2 of these tumors regressed again after hormone injections were stopped. When virgin mice were given hormone injections with 5-HT, all 6 treated mice developed tumors at an earlier age (75 and 60 wk for hormone and hormone-and-5-HT-treated mice, resp.) than in untreated controls, where the average age at tumor development was 94 wk. Once they had appeared, all tumors grew independently of further hormone stimulation. When virgin mice were given hormone injections as above but without prolactin and with increased progesterone, tumors again appeared at a lower age than in controls. When 11 virgin mice were given pituitary implants under the kidney capsule at 10 wk of age, all 11 developed mammary tumors at a mean age of 58 wk, while only 4 of 10 untreated mice developed tumors, at a mean age of 83 wk. When the pituitary implant was removed from 6 mice (bearing 7 tumors), 3 tumors continued to grow, 1 remained the same, and 3 regressed. When hormone injections were combined with pituitary implants, the average age at tumor development was not lowered significantly from that at which tumors began to appear in mice given pituitary grafts without hormone treatment. The development and early age of tumor appearance in mice given pituitary implants was not reduced in ovariectomized mice given pituitary grafts.

1216 EPIDERMAL CHALONE AND CELL PROLIFERATION IN A TRANSPLANTABLE SQUAMOUS CELL CARCINOMA IN HAMSTERS: I. *IN VIVO* RESULTS. (E.) Elgjo, K. (Rikshosp., Oslo, Norway) and H. Hennings. *Virchow Arch Zellpath* 7(1):1-7, 1971.

The effects of a partially purified pig skin extract containing the growth regulating factor, epidermal

chalone, on the growth parameters of a transplantable keratinizing hamster epithelioma were studied. Five tumor-bearing hamsters were injected i.p. with 50 mg chalone and vinblastine (VB, 1.5 mg/kg) or 50 mg liver powder and VB, or VB only; the animals were sacrificed 4 hr later and mitoses in the tumor was inhibited 34% in the chalone-treated animals compared to the controls. DNA synthesis was depressed 84% at 8 hr after chalone injection compared to liver extract injection. Mitotic duration in livers treated with liver powder, chalone or VB was 0.6 hr, 0.9 hr and 0.8 hr, resp. Three daily i.p. injections of 50 mg of chalone into tumor-bearing animals resulted in small ulcerations at the site of injection, but no regression of tumors was observed.

- 1217 HISTOCHEMICAL STUDIES ON MUCOSUBSTANCE IN HUMAN GASTRIC CARCINOMA. (E.) Sugimoto, A. (Hiroshima U. Sch. Dent., Japan) and K. Kirimoto. *Acta Histochem Cytochem* 3(3):81-104, 1970.

The histochemical properties of the gastric mucosa of human gastric carcinomas were investigated; case material included 65 specimens of early gastric carcinoma, 135 cases of advanced carcinoma, 50 non-cancerous lesions, and 20 specimens of normal mucosa from duodenal and rectal tissue. Tissue sections were prepared and stained with any of 10 different stains, including mucicarmine, alcian blue-periodic acid-Schiff reaction (AB-PAS), alcian blue, azure eosin, and hematoxylin eosin. Two different types of mucosubstances with different staining properties occurred in normal and non-cancerous gastric mucosa: mucosubstances which stained pink in the periodic acid-Schiff reaction alone when the AB-PAS reaction was applied and which did not stain with alcian blue, mucicarmine, or metachromasia; and mucosubstances which stained with alcian blue alone or with both alcian blue and periodic acid-Schiff in the AB-PAS reaction and which stained intensely with mucicarmine and toluidine blue. These 2 mucosubstances were characteristic of the gastric mucosa proper (e.g., the cardiac, corporal and pyloric regions) and of the region of intestinal metaplasia (e.g., the area characterized by goblet cells), resp. Histochemically, most gastric carcinomas were of the latter type; 78% of tissue preparations from cancer patients were stained with the AB-PAS reaction and were positive for both alcian blue and periodic acid-Schiff. Early and advanced gastric carcinomas had similar staining properties, with 78.5% of cases in each stage belonging to the goblet-type mucosubstance category. Of 114 tubular adenomas, 57 showed "marked" goblet-cell type mucosubstance staining, and 24 showed gastric mucosa proper type mucosubstance staining. Of mucocellular carcinomas, 14 were of the goblet-cell type and none were gastric mucosa proper staining type. Of 14 papillary adenocarcinomas, 7 were of the goblet cell type and 7 were of the gastric mucosa proper type. Apparently, intestinal metaplasia may be a background change of gastric carcinoma.

- 1218 HODGKIN'S DISEASE: ONE ENTITY OR TWO? (E.) Smithers, D. W. (Roy. Marsden Hosp., London, England). *Lancet* 2(7686):1285-1288, 1970.

The age-distribution of 475 patients with Hodgkin's disease was investigated in order to test the hypothesis that this condition represents 2 disease entities, including an inflammatory condition and neoplastic condition. That hypothesis is based on the bimodality of the age-incidence curve for Hodgkin's disease, in which peaks occur for males at age 35-50 yr and 55-60 yr. In the present survey, age-incidence peaks occurred at age 25-26 yr and 51-55 yr for all patients; the peaks for males were more pronounced than for females, who were seen to have a less prominent late age peak than males. When 414 cases were classified into a less malignant lymphocytic group and a more malignant mixed-cellularity, intermediate, and lymphocytic depletion group, it was found that the bimodality of the age-incidence curve was preserved for men. Age peaks for the less malignant form of Hodgkin's disease occurred at age 26-30 yr and 51-55 yr. Age peaks in the more malignant groups occurred at age 30-31 yr and 56-60 yr. The age-incidence curve for the nodular-sclerosis type of Hodgkin's disease showed only the early peak, and these curves were similar for both men and women. The findings appear to suggest that Hodgkin's disease is a single progressive neoplastic condition, unified from lymphocytic predominance through mixed cellularity to lymphocytic depletion. The bimodality of the age-incidence curve might be explained by the development of host immunity which leads to the nodular-sclerosis pattern and, in some cases, by regression of the disease in its second stage.

- 1219 CYTOGENETIC ANALYSIS OF MULTINUCLEATE ASCITIC TUMOR IN GOLDEN HAMSTERS. (E.) Shidoy, T. (Framingham Union Hosp., Mass.), T. H. Ingalls and A. Herranen. *Arch Environ Hlth* 22(1):141-150, 1970.

Chromosome patterns of an ascitic fluid sarcoma that had been induced by 3-methylcholanthrene in the hamster in 1951 were analyzed. Metaphase plates recovered from the serous fluid of 11 animals revealed a modal number of 96 compared to the expected 44 in normal animals, and the DNA content of the tumor cells was higher than that of normal thymus tissue (22.4 vs 6.8 $\mu\text{g}/10^6$ cells). Karyotype analysis (standard grouping of the 2 sex chromosomes and 6 morphologically distinct autosomal groups) of 38 metaphase plates from the ascitic tumor revealed hyperploidy (to various degrees) in all except the D group which was hypoploid (5 or 6 chromosomes instead of the expected 8). Members of the F group demonstrated a definite trend toward trisomy.

- 1220 CHROMOSOME ABERRATIONS IN FANCONI ANEMIA. (E.) Visfeldt, J. (Commun. Hosp., Copenhagen, Denmark) and E. Mortensen. *Acta Path Microbiol Scand* 78(5):545-550, 1970.

The diagnosis of Fanconi's aplastic anemia in a 7-yr-old girl was confirmed by chromosome analysis: the girl died of her condition within a year after initial admission to the hospital. X-ray examination of her ossification centers showed development

corresponding to that of a 2-yr-old. Chromosome analysis revealed aberrations of the chromatid type; no dicentrics, tracentrics or rings were found. There were no mitoses in endoreduplication, and only a few tetraploid cells were seen. The patient showed 34% of cells with structural abnormalities, as compared to 2% of abnormal cells in the blood of 1 of her parents. She had 22% chromatid gaps and isochromatid gaps (compared to 1% for a normal parent); chromatid exchanges were observed in 9% of cells (compared to 0% in a normal parent.) Fanconi's anemia has been correlated with an increased tendency to develop leukemia and other neoplastic diseases; it is suggested that the chromosome aberrations noted in Fanconi's anemia may predispose patients to changes induced by carcinogenic agents.

1221 THE RISK OF LUNG CANCER IN MALES WITH BULLOUS DISEASE OF THE LUNG. (E.)

Stoloff, I. L. (Philadelphia Dept. Publ. Hlth., Pa.), P. Kanpfsky and L. Magilner. *Arch Environ Hlth* 22(1):163-167, 1970.

The association between bullous disease and lung cancer was investigated in 49,902 persons appearing at the Central Philadelphia Mass Radiography Unit in a 7 month period. Of 17,708 males without lung bullae, there were 34 with proved primary lung cancer; of 49 men with lung bullae, there were 3 with cancer. The prevalence rate of cancer among men without bullae was 1.9/1000, compared to a prevalence rate of 61/1000 for men with bullae. The relative risk of contracting cancer in white men was calculated as 40, while the relative risk of cancer for nonwhite men was calculated as 27. No women appeared in the survey having both bullous disease and lung cancer. A retrospective survey of all men with lung cancer presenting at the Unit since 1947 showed that prevalence rates of bullous disease in 890 men with cancer were 12.1/1000 (white) and 54.2/1000 (nonwhite).

1222 TYROSINE HYDROXYLASE ACTIVITY IN A TRANS-PLANTABLE ISLET CELL TUMOR OF GOLDEN HAMSTER. (E.)

Axelsson, S. (Inst. Anat. Histol., U. Lund, Sweden), L. Cegrell and A. M. Rosengren. *Experientia* 26(9):998-999, 1970.

Islet cell tumors in hamsters were examined for the presence of an enzyme system catalyzing the conversion of tyrosine to dopa. Islet cell tumors were transplanted to adult hamsters of both sexes and allowed to grow for 4-12 wk; 22 tumors were analyzed for tyrosine hydroxylase activity. Three tumors contained 3,4-dihydroxyphenylacetic acid, and 9 contained 3-methoxy-4-hydroxyphenylacetic acid, both endogenous dopamine metabolites. Tyrosine hydroxylase enzyme which converts tyrosine to catechol derivatives in the islet cell tumors was present in amounts of 20 nmole/g/hr. Tetrahydrofolic acid increased the enzyme activity by 340% compared to controls, while 2,2'-bipyridyl decreased enzyme activity to 18% of control values. The rapid turnover of dopamine could explain the occurrence of 3-methoxy-4-hydroxyphenylacetic acid in the tumor; the latter compound is usually present in tumors

derived from the neural crest, including neuroblastoma, ganglioneuroma, and pheochromocytoma.

1223 THE POTENTIALITY OF OUT-OF-CYCLE ACUTE LEUKEMIA CELLS TO SYNTHESIZE DNA. (E.)

Stryckmans, P. (Jules Bordet Inst. Ctr. Tumor, Free U. Brussels, Belgium), G. Delalieux, J. Manaster and M. Socquet. *Blood* 30(6):697-703, 1970.

The fraction of nonproliferating acute leukemic cells which retain the ability to synthesize DNA was determined. Venous blood from 18 patients with acute leukemia was exposed to UV light for 30 sec, and DNA synthesis as measured by uptake of ^3H -thymidine was observed. Incorporation of ^3H -thymidine revealed the fraction of leukemic cells in normal DNA synthesis (S-cells). The percentage of ^3H -thymidine labeled non-S (out of cycle, in G_1 or G_2) circulating leukemic blasts in the UV-exposed samples ranged from 94-100%, with the exception of 1 case with 70%, a patient who had undergone chemotherapy with daunomycin and vincristine until 3 days before the experiment. In cells not exposed to UV, the amount of non-S cells incorporating ^3H -thymidine was zero. The DNA synthesizing activity of the UV exposed cells probably represented DNA repair replication. Apparently, the nonproliferating acute leukemia blasts were not cells which have stopped dividing at maturation ("end cells"), but resting cells.

1224 CYTOLOGIC STUDIES OF TUMORS: L. CLONAL PROLIFERATION OF FOUR STEMLINES IN THREE HEMATOPOIETIC TISSUES OF A PATIENT WITH RETICULOSARCOMA. (E.)

Obara, Y. (Hokkaido U., Sapporo, Japan), M. Sasaki, S. Makino and C. Mikuni. *Blood* 37(1):87-95, 1970.

Peripheral blood, lymph node tissue, and bone marrow from a 47-yr-old female with reticulosarcoma were examined cytologically to detect chromosome irregularities associated with this condition. Four chromosomally different cell lines were found in the 3 tissues examined. Each line had a similar karyotype marked by trisomy for E_{16} , E_{17} and E_{18} , and the loss of A_1 , two F and two 4 C elements; M and R markers were also found. Lymph node cells showed an abnormal chromosome picture in 4 of 70 cells examined; abnormal cells were characterized by M_1 , R_1 and R_2 markers and trisomy for E_{16} - E_{18} , and the loss of A, F and C elements, as above. In peripheral blood not stimulated with phytohemagglutinin, 60% of cells had M_1 , M_2 , M_3 , and R_1 markers, trisomy for E_{17} and E_{16} , and the characteristic loss of A, F and C elements. These cells may have been derived from the lymph node cell line. Bone marrow cells had M_1 and M_4 markers, trisomy for E_{16} - E_{18} , and loss of A, F, and C elements. Peripheral blood had the highest variability in malignant cells. On the basis of the similarity in the marker chromosomes in the cell lines, the original stem line of the 4 may have been the line from the lymph node, perhaps the primary site of the malignancy.

- 1225 HYPOESTROGENISM AND ENDOMETRIAL CARCINOMA. (E.) Liu, W. (Youngstown Hosp. Ass., Ohio). *Acta Cytol* 14(9):583-585, 1970.

The cytohormonal status of patients with endometrial carcinoma and the possible relationship between cytohormonal effect and the exfoliation of endometrial carcinoma cells was investigated. Subjects were 200 patients with primary endometrial cancer diagnosed as having adenocarcinoma or adenoacanthoma of the endometrium and ranged in age from 38-77 yr. Vaginal aspiration smears were taken, and the cytohormonal effect was assessed and expressed as percentages of superficial, intermediate and parabasal squamous cells in the smears. Sixty-two percent of the patients had a minimum of superficial cells, 28% had a moderate number, and 10% had a large number. Fifty-two percent of patients had minimal cytologic hypoestrogenism, 10% had moderate hypoestrogenism and 38% had severe hypoestrogenism. Among patients with 20% or more exfoliated superficial squamous cells, 92% had definite or suspected tumor cells; and among patients with 80% or more intermediate cells, only 60% had tumor cells. Since endometrial carcinoma cells were not as often found in parabasal or intermediate cell smears as in smears with many superficial cells, it was concluded that the association between cytologic hypoestrogenism and endometrial carcinoma is not as clear as has been believed.

- 1226 MAMMARY TUMOR DEVELOPMENT IN BR6 MICE: OVARIAN INFLUENCES AND 5-HYDROXYTRYPTAMINE. (E.) Lee, A. E. (Imperial Cancer Res. Fund, London, England). *Brit J Cancer* 24(3):561-567, 1970.

The importance of ovarian influences during early pregnancy on tumor development was studied by observations in pregnant and pseudopregnant mice and in mice injected with 5-hydroxytryptamine (5-HT). Ninety-three percent of new tumors appeared after the 12th day of pregnancy, the mean time of tumor appearance being 17 days. New tumors which subsequently regressed after parturition appeared later than those which showed incomplete regression, the first group appearing after a mean of 18 days of pregnancy, and the second group of tumors appearing after a mean of 16 days. Tumors which regressed completely after parturition recurred by the 12th day after the next pregnancy in 64% of cases, while tumors which showed only partial regression after parturition resumed growth earlier, 66% recurring before day 12. Female mice made pseudopregnant by pairing with vasectomized males showed 12 instances of recurring tumor during 4 cycles of pseudopregnancy; 9 tumors did not recur, and 3 new tumors appeared. Apparently, pseudopregnancy may stimulate the growth of an established regressed tumor, but does not produce new tumors. Alkaline phosphatase activity in normal mouse mammary glands showed a uniform increase in growth during pregnancy without a marked increase at any particular time. Newly pregnant mice were given injections of 3.0 mg of 5-HT to terminate pregnancy, with the result that treated mice seemed to develop tumors earlier than usual, often during the second preg-

nancy. However, no difference in tumor development was observed between control and 5-HT-treated virgin females, treated mice developing tumors in 13/22 cases, and untreated controls developing tumors in 8/16 cases. Apparently, while 5-HT may have influenced tumor development in breeding mice, it had no effect on virgins.

- 1227 ULTRASTRUCTURE OF GLOMUS TUMORS AND ARTERIOVENOUS GLOMERULA. (Ger.) Lüders, G. (U. Clin. Tubingen, Germany), W. Schlote and M. Reinhard. *Arch Klin Exp Derm* 238(4):398-416, 1970.

Ultrastructural findings on surgical specimens from a glomus tumor of a 34-yr-old patient from a family with dominant autosomal hereditary multiple glomus tumors are presented. A variety of epithelioid cells seem to be histogenetically derived from smooth muscle cells. These epithelioid cells must have lost their characteristic myofilaments centrifugally during transformation; they present now a light perinuclear halo populated with organelles. These cells are never found at the direct border of the vascular lumen where a thin layer of active endothelial cells is usually present. Large amounts of histiocytes and mast cells are usually found along with the endothelial cells. The existence of a functional relationship between the endothelial, mast cells and histiocytes is assumed and the term of "myoepithelioid" cells is suggested for the light cells to indicate their histogenetic origin.

- 1228 CARCINOMA OF THE OESOPHAGUS AND GASTRIC SURGERY. (E.) MacDonald, J. B. (Gen. Hosp. Nottingham, England), J. G. Waissbluth and M. J. S. Langman. *Lancet* 1(7688):19-20, 1970.

The hypothesis that gastric surgery, especially surgery for peptic ulcer, predisposes to cancer of the esophagus was tested in 203 patients with esophageal cancer and in 208 patients with rectal cancer. Of the patients with esophageal cancer, 73% had squamous cell tumors, 4% were anaplastic, and 2.5% had adenocarcinomas. Two percent of esophageal cancer patients had undergone previous gastric surgery, and 4 patients had achalasia of the cardia. One percent of rectal cancer patients had histories of gastric surgery. The operations performed were gastrectomy using the Billroth procedure. The finding failed to confirm a clear association between gastric surgery and esophageal cancer.

- 1229 THE DEVELOPMENT OF "SPONTANEOUS" NEOPLASTIC TRANSFORMATION *IN VITRO* OF CELLS FROM YOUNG AND OLD MICE. (E.) Franks, L. M. (Imperial Cancer Res Fund, London, England) and S. Henzell. *Europ J Cancer* 6(5):357-364, 1970.

The capacity of cell lines established in culture from various mouse tissues to produce tumors when injected in syngeneic mice was investigated. Cell lines were initiated from tissues of embryo mice, young mice, and aged mice; explants were taken from kidney, bladder, brain, lung and heart. Cells were inoculated into mice (3×10^6 cells) after periods

in culture varying from 90 days to more than 2 yr. The length of the slow growth phase in culture before the onset of rapid *in vitro* cell growth was recorded. Six of 14 cell lines from young mice and 10 of 21 lines from old mice produced tumors on s.c. inoculation into mice after periods in culture ranging from 190-638 days. Latent periods for tumor development ranged from 15-316 days. The tumor developing capacity of cell lines was apparently not related to the length of the slow growth rate of the cells. No relationship was found between tumorigenicity and strain or age of the donor tissue, method of initiation or transfer of cultures. Ten of the tumor-producing cell lines had already undergone malignant change before 200-250 days in culture.

- 1230 CHROMOSOMAL DNA REPLICATION PATTERN IN HUMAN TUMOR CELLS *IN VITRO*. (E.) Kucheria, K. (All-India Inst. Med. Sci., New Delhi, India). *Brit J Cancer* 24(3):484-488, 1970.

In vitro tritiated thymidine labeled human solid tumor cells were examined for chromosome DNA replication patterns at the terminal stages of the S-period in cell lines of male and female origin. Cell lines used from rhabdomyosarcoma revealed karyotypic diversity with the appearance of marker chromosomes. In cell lines of female origin heavily labeled median size chromosomes of the group XX6-12 appeared while in those of male origin one of the chromosomes of group 21-22Y appeared more heavily labeled. In all cell lines (rhabdomyosarcoma, astrocytoma, neuroblastoma) one of the chromosome pair of group 13-15, pair no. 17 and chromosomes of the groups 19-20 and 21-22 showed early termination of their DNA synthesis. DNA replication of chromosomes in neoplastic cells is basically unchanged despite changes in chromosome number and morphology with no significant relationship of age of patient or origin of neoplastic cells to this pattern.

- 1231 CYTOPLASMIC DESMOSOMES IN NEOPLASTIC KERATINOCYTES OF SQUAMOUS CELL CARCINOMA. (Ger.) Klingmuller, G. (U. Clin. Bonn, Germany), H. U. Klehr and Y. Ishibashi. *Arch Klin Exp Derm* 238(4):356-365, 1970.

The presence of intracytoplasmic desmosomes in de-differentiated keratinocytes from specimens of 6 surgically removed squamous cell epithelial carcinomas was ascertained by electron microscopy. These desmosomes appeared to be highly differentiated and identical to normal desmosomes; they were referred to as "desmosome equivalents" and their length was 0.35-1.2 μ . The desmosomes appeared either singly or in filamentous structures suggesting that their formation may occur independently of the cell membrane. The presence of rough endoplasmic reticulum close to the nucleus of the neoplastic keratinocyte indicated an intensification of metabolic processes. The cell surface of the transformed keratinocytes exhibited very few desmosomes but presented an increased amount of microvilli hindering the occurrence of normal inter-cellular contacts within the tissue.

- 1232 INHIBITION OF WALKER 256 CARCINOSARCOMA GROWTH BY DIETARY ZINC DEFICIENCY. (E.) DeWys, W. (U. Rochester Sch. Med. Dent., N.Y.), W. J. Pories, M. C. Richter and W. H. Strain. *Proc Soc Exp Biol Med* 135(1):17-22, 1970.

The effect of a zinc-deficient diet on the development, growth, and survival from Walker 256 carcinoma was investigated. Rats fed on normal diet, zinc-supplemented diet, and zinc-deficient diet were given i.m. injections of 2×10^6 Walker carcinoma cells. The median survival time for rats fed with the normal diet was 18.5 days after injection of the tumor cells, while the mean survival time for rats on a zinc-deficient diet was 46 days. In rats fed normal or zinc-supplemented diets, 23-25/25 of the rats had died before day 60, while only 12/25 of the rats on the zinc-deficient diet were dead at this time. Five rats in the zinc-deficient group remained tumor-free at day 60; while all living rats in the other experimental groups had tumors by this day. The growth of tumors in zinc-deficient rats was markedly decreased compared to tumor growth in rats on the normal diet or rats on the zinc-supplemented diet; by day 15 average diameters of tumors in normal-fed, supplemented zinc-fed, and deficient zinc-fed rats were 3.1, 2.8 and 1.1 cm, resp.

- 1233 PROTEIN-BOUND CALCIUM IN TUMORS. (E.) Anghileri, L. J. (Essen Tumor Res. Clin., U. Essen, Germany). *Naturwissenschaften* 57(11):547-548, 1970.

Levels of protein-bound calcium in lymphosarcoma- and Ehrlich carcinoma-bearing animals were determined. Animals bearing s.c. transplants of lymphosarcoma or Ehrlich carcinoma were given i.p. injections of 10 μ C of $^{45}\text{CaCl}_2$, killed 24 hr later, and assayed for calcium in blood, liver and kidney. More labeled calcium was found in supernatants from normal animals than in supernatants from tumor-bearing animals. Values for ^{45}Ca in blood of lymphosarcoma-bearing animals were 2.3%, and for controls, 5.5%. Values for the blood of Ehrlich carcinoma-bearing animals were 2.7% and, for random-bred albino controls, 4.6%. However, liver and kidneys of Ehrlich carcinoma-bearing animals contained more ^{45}Ca than did liver and kidneys of controls, probably because this tumor is high in soluble proteins.

- 1234 EXPERIMENTAL RETINOBLASTOMA: I. MORPHOLOGY AND BEHAVIOR OF CELLS CULTIVATED *IN VITRO*. (E.) Huang, L. H. (Wills Eye Hosp. Res. Inst., Philadelphia, Pa.), T. W. Sery, M. M.-S. Chen, A. S. M. Cheung and A. H. Keeney. *Amer J Ophthalmol* 70(5):771-777, 1970.

The growth in culture of cells from 9 cases of human retinoblastoma was investigated. While all 9 cultures remained viable for more than 2 yr, 4 showed proliferation after transfer, and 5 simply maintained viability. Cultures were apparently comprised of cell types divisible into 4 categories: microglial and glial cells, ganglion cells, large polygonal cells with no dendritic processes and pleomorphism

of nucleoli, and large elongated cells resembling fibrocytes. All of these cell types may have been derived as aberrant variations of the malignant cells of retinoblastoma. One culture was transferred in 60 serial passages and may be a malignant strain containing the original retinoblastoma cell type. When cultured retinoblastoma cells were injected in neonatal rabbits and mice, no lesions were observed either at the inoculation site or at microscopy.

- 1235 CHROMOSOMES AND CAUSATION OF HUMAN CANCER AND LEUKEMIA: VI. BLASTIC PHASE, CELLULAR ORIGIN, AND THE Ph¹ IN CML. (E.) Sandberg, A. A. (Roswell Park Mem. Inst., Buffalo, N. H.), D. K. Hossfeld, E. Z. Ezdinli and L. H. Crosswhite. *Cancer* 27(1):176-185, 1971.

The incidence of Ph¹ chromosome-negative cells in patients with chronic myelocytic leukemia was investigated in a survey of 107 cases. Of these patients with chronic myelocytic leukemia, 79 were Ph¹-positive; most Ph¹-negative patients were elderly (60-yr-old or more) while most Ph¹-positive patients were younger (50-yr-old or less). In 6 patients with Ph¹-positive chronic myelocytic leukemia, marrow cells were Ph¹-negative prior to any therapy in some and after treatment of various types in others. In these patients, the M:E ratio was high, ranging from 2-240:1. The observation of Ph¹-negative cells in some patients with chronic myelocytic leukemia would seem to cast doubt on the hypothesis of a unicellular stem cell origin for Ph¹-positive cells in chronic myelocytic leukemia.

- 1236 THE PATTERN OF CELL GROWTH IN RETICULUM CELL SARCOMA AND LYMPHOSARCOMA. (E.) Peckham, M. J. (Roy. Marsden Hosp., Sutton, Surrey, England) and E. H. Cooper. *Europ J Cancer* 6(5):453-463, 1970.

The pattern of cell proliferation in human reticulum cell sarcoma and lymphosarcoma are reported based on labeling studies and DNA measurement in fresh lymph-node biopsy tissue. Tumor cell labeling indices were between 20 and 40% in all but one biopsy in reticulum cell sarcomas and showed considerable variation in lymphosarcomas with an accumulation of cells in the G₂ phase or a hold-up in the S phase. No correlation could be established between labeling index and patient response to treatment. Hypotetraploid reticulum cell sarcomas tended to localize to one or two lymph-node areas whereas tumors showing modal DNA contents in the diploid range tended to diffuse and result in generalized disease.

- 1237 CONCURRENT INFECTIOUS MONONUCLEOSIS AND ACUTE LEUKEMIA. (E.) Freedman, M. H. (Child. Hosp. Los Angeles, Calif), G. H. Gilchrist and G. D. Hammond. *JAMA* 214(9):1677-1680, 1970.

Nine patients with concurrent infectious mononucleosis (IM) and acute leukemia were observed, and 4 cases were described. The age of the patients at diagnosis of leukemia ranged from 3.75-35 yr; 7 of the cases were males. Eight of the cases were

diagnosed as acute lymphatic leukemia; the 35 yr-old patient had acute monocytic leukemia. IM was diagnosed from 3 months to 3.75 yr after the diagnosis of leukemia in 7 cases, and 3 and 3½ months before the diagnosis of leukemia in 2 cases. Heterophil antibody titers ranged from 1:112-1:896 before and after guinea pig kidney absorption. The etiological relationship of IM and acute lymphatic leukemia remains unclear.

- 1238 VAGINAL TRICHOMONIASIS AND PRECANCEROUS STATES OF THE CERVIX: A PRELIMINARY REPORT. (E.) de Carneri, I. (U. Padua, Italy) and Di Re, F. *J Obstet Gynec Brit Comm* 77(11):1016-1018, 1970.

The incidence of vaginal trichomoniasis infection among women with normal and precancerous vaginal smears was investigated. The case material was comprised of 1732 vaginal smears from adult women in a town in Northern Italy. Scrapings from the ectocervix and an endocervical swab were grown in cysteine-peptone:liver-maltose medium; smears were divided into 5 classes ranging from normal cytology to neoplastic cytology (Papanicolaou). *Trichomoniasis vaginalis* was found in 315 subjects or 18.2% of those examined. Seventy-four percent of the smears were classified as Class I (normal cytology). Less than 34% of the expected incidence of trichomoniasis infection was seen in Class I smears while 94% of the expected incidence in Class II smears was observed. More than 234% of the expected incidence of infection was found in Class III vaginal smears, which were characterized by dyskaryosis and basal cell hyperactivity. More than 119% of the expected number of infections occurred in smears from Classes IV and V; smears in these classes have the morphological properties of neoplastic cells. On the basis of these findings, it appears plausible to suggest that there is a relationship between cervical neoplasia and *Trichomoniasis vaginalis* infection.

- 1239 BLUE NEVUS OF THE PROSTATE GLAND. (E.) Jao, W. (Michael Reese Hosp. Med. Ctr., Chicago, Ill.), D. F. Fretzin, M. L. Christ and L. M. Prinz. *Arch Path* 91(2):187-191, 1971.

Ultrastructural studies in a case of blue nevus of the prostate gland are described. A multinodular prostate weighing 35 g was removed from a 76-yr old white man; the gland was diffusely gray in color with dark brown streaks and showed characteristic features of benign hyperplasia under light microscopy. The fibromuscular stroma was extensively infiltrated with stellate and spindle-shaped cells with finely granular brown cytoplasmic pigment which stained positively with the Masson-Fontana stain, but negatively with Prussian blue. Electron microscopic examination showed numerous electron-dense coarse granules diffusely distributed in the cytoplasm of spindle-shaped cells; the morphology of these granules was typical of mature melanosomes. Several granules resembling premelanosomes were also observed. The prostatic lesion in this case appears to be histologically analogous to the common blue nevus as opposed to the cellular blue nevus of the skin.

- 1240 THE CYTOLOGY, DISTRIBUTION AND FUNCTION OF THE NEOPLASTIC CELLS IN LEUKEMIA RETICULO-ENDOTHELIOSIS. (E.) Berg, B. (U. Hosp. Lund, Sweden) and L. Brandt. *Scand J Haemat* 7(6):428-434, 1970.

The characteristics of neoplastic cells found in aspiration biopsy from peripheral blood, bone marrow, spleen, liver, and lymph nodes of patients with leukemic reticuloendotheliosis were investigated. Biopsy material was obtained from 4 male patients aged 35-55 yr. Neoplastic cells found in material from the various sites were similar morphologically. In all cases, cells were round and about twice the size of normal lymphocytes; nucleoli were uncommon, as were mitoses, and the cytoplasmic margin had many villous particles. In all cases, spleen and liver material contained a higher proportion of neoplastic cells than blood and bone marrow. The amount of neoplastic cells in liver and spleen samples reached maximum values of 80% and 88%, resp., while maximums for blood and bone marrow did not exceed 55% and 60%, resp. There was no convincing evidence of phagocytosis of neoplastic cells in the peripheral blood of any patient. Incorporation of ^3H -thymidine by neoplastic cells was also low, possibly indicating that the neoplastic tissue had low proliferative capacity.

an evaluation of 22,000 neuroblastoma cells, 126 tumor cells were found in mitosis; the overall mitotic index was 0.572%. The change in the labeling index and in labeling intensity of neuroblastoma cells was a function of time after ^3H -thymidine injection. Percentage of labeled mitoses rose from 10-90 between 1-7 hr after label injection, subsequently decreasing to a low of 15% at 35 hr post-injection. Data from labeled mitoses indicated a minimum G_2 phase time of 1-2 hr and a mean DNA synthesis time of about 27-28 hr. At 1½ hr after ^3H -thymidine injection, 11% of all neuroblastomas were labeled and 53, 18, and 1.3%, resp., of cells with large, intermediate, and small nuclei were labeled. The neuroblastoma cells seem to comprise 2 populations (one, which was initially labeled, of proliferating cells with large nuclei and one, which was initially unlabeled, of non-proliferating cells with small nuclei); the non-proliferating state appears to be temporary, and the majority of tumor cells seem to be able to undergo cell division.

- 1243 FACILITATION OF RAT MAMMARY TUMOR GROWTH BY BCG. (E.) Piessens, W. F. (Massachusetts Gen. Hosp., Boston), F. L. Lachapelle, N. Legros and J. C. Heuson. *Nature* 228(5277):1210-1211, 1970.

The effect of administration of bacillus Calmette-Guerin (BCG) to rats bearing mammary tumors induced by 7,12-dimethylbenz(a)anthracene (DMBA) was investigated. Rats were given a single s.c. dose of 1 mg BCG when 1 mammary tumor had developed following treatment with the carcinogen. BCG did not affect the primary tumors; but the total tumor surface/rat, the number of tumors/rat, and the number of rats developing new tumors were significantly higher in the BCG-treated group. At 4 wk after 7,12-dimethylbenz(a)anthracene injection, 6 new tumors had developed in controls and 17 in BCG-treated animals. At 5 wk after carcinogen-treatment, 3 controls and 13 BCG-treated rats had developed new tumors. At 6 wk after carcinogen treatment, total new tumor area/rat was 85 cm² for controls and 325 cm² for BCG-treated rats. Facilitation of tumor growth by BCG may be accounted for by immunological tumor enhancement.

- 1244 DIABETES MELLITUS AND CANCER. (E.) Anonymous. *Brit Med J* 4(5729):191, 1970.

A survey of the data on the association of diabetes mellitus and cancer of various sites indicates that 13% of cancer patients with diabetes have cancer of the pancreas in 1 study. Recent studies, however, have shown that among men with diabetes, death from cancer of all types other than pancreatic cancer is less frequent than expected; deaths from rectal and respiratory tract cancer were especially rare in diabetics. Among women with diabetes, death from cancer was slightly more frequent than expected and probably hid an increased risk of cancer of the pancreas and cancer of the uterus. The observation of pancreatic duct hyperplasia in diabetes may point to a common etiology for diabetes and pancreatic cancer.

- 1241 CHANGES IN CELLULAR PROPERTIES DURING THE LONG-TERM SERIAL CULTURE OF LUNG CELLS OF NEWBORN HAMSTER AND THE TRANSFORMATION INTO A CELLS. (E.) Matsuya, Y. (Res. Inst. Tuberc. Leprosy Cancer, Tohoku U., Sendai, Japan) and I. Yamane. *Tohoku J Exp Med* 102(1):37-49, 1970.

Cellular properties, morphology, and karyotypic changes were followed during the course of cell establishment of neonatal hamster lung cells. After 23 transfers, cells that had been grown in a serum albumin fortified (BSA) medium became capable of sustaining a constant stable growth in the presence or absence of albumin (until after 90 transfers the growth promotion of albumin was negligible), and after 27 transfers the cells exhibited an ability to grow at low inoculation densities (300 cells/plate). Chromosomal studies of the cells revealed that the typical diploid karyotype persisted after the cells demonstrated the capacity to grow at low inoculum density until the 37-44th transfers when the karyotype shifted at the tetraploid range with a modal number of 45, and the cells acquired a neoplastic morphology at the 70th transfer.

- 1242 CELL PROLIFERATION IN NEUROBLASTOMA. (E.) Wagner, H. P. (U. Hosp., Berne, Switzerland) and H. Käser. *Europ J Cancer* 6(5):69-372, 1970.

The proliferation of neoplastic cells was investigated in cells from a female patient with generalized neuroblastoma. Tumor cell samples were taken from different parts of a superficially growing metastasis. Labeling index, median grain-count and mitotic index were estimated by autoradiography after pulse-labeling with tritiated thymidine. In

- 1245 HEREDITARY POLYPOSIS OF THE COLON. (E.) Wyndham, N. (Newtown, New South Wales, Australia). *Med J Aust* 57(19):866-869, 1970.

Hereditary polyposis of the colon expressed in 4 generations of an Australian family was examined. The polyposis gene has been described as a dominant gene transmitted to about half the children of a parent possessing it. In the 34 members of the family examined, 2 had polyposis and 8 had polyposis with carcinoma. All 3 of the first generation father's children had polyposis and carcinoma, and 4 of the 12 members of the third generation had polyposis with carcinoma. Symptoms of polyposis had their onset in the fourth and sixth decades of life for the members of the family for whom data are available. Carcinomas arising in connection with polyposis in this family were located in the colon, rectum, or anus.

- 1246 ANNULATE LAMELLAE IN HUMAN PARATHYROID ADENOMA. (E.) Boquist, L. (Inst. Path., U. Umea, Sweden). *Virchow Arch Zellpath* 6(3):234-246, 1970.

Ultrastructural examination of 2 human parathyroid adenomas revealed annulate lamellae in the tumor cells. The patients, a middle-aged man and woman, had tumors in 1 of the lower parathyroid glands, and both had symptoms of hyperparathyroidism. Tumors were composed mainly of chief cells and a few oxyphil cells; these cells showed an abundance of mitochondria. Nuclei of chief cells were of varying sizes and occasional giant nuclei were observed; in some cases prominent Golgi bodies and endoplasmic reticulum were seen. Annulate lamellae were often seen in the chief cells, but seldom in oxyphil cells; they occurred both in the perinuclear region of cells, and in other regions of the cytoplasm. No intranuclear lamellae were observed. Annulate lamellae were composed of parallel arrangements of double membranes in straight, curved, semi-circular or circular configurations; membranes were smooth-surfaced and merged at times to form pores. In transverse section, lamellae were cylindrical with electron-dense peripheral areas and less dense interiors. Individual lamellae were often separated by electron lucent spaces with cisterns of granular endoplasmic reticulum situated at the ends of, or around, the lamellae. Circular or semi-circular lamellae sometimes encompassed cytoplasmic ground substance or amorphous material of varying electron opacity. Mitochondria were often completely or partially confined within lamellae.

- 1247 CHROMOSOMAL EVIDENCE FOR THE SECONDARY ROLE OF FIBROBLASTIC PROLIFERATION IN ACUTE MYELOFIBROSIS. (E.) Van Slyck, E. J. (Henry Ford Hosp., Detroit, Mich.), L. Weiss and M. Dully. *Blood* 36(6):729-735, 1970.

Cytogenetic studies were performed on myeloblasts derived from the peripheral blood of a 22-yr-old white female with acute myelofibrosis and agnogenic myeloid metaplasia in order to determine whether

fibroblastic proliferation associated with acute myelofibrosis is a primary or a secondary feature of the disease. Chromosome analyses were carried out on 24 cells, showing a consistent abnormality. In the A group, the number 2 chromosomes were normal, but only 1 normal number 1 chromosome was seen, and there was a marker chromosome larger than the normal number 1 but with a submetacentric centromere. Only 1 number 3 chromosome was seen, and there was an extra submetacentric chromosome the size of a C group chromosome. These abnormalities were interpreted as a 1-3 translocation. The patient's bone marrow fibroblasts were normal karyotypically, as were her lymphocytes. Apparently, the basic abnormality in acute myelofibrosis is not fibroblastic proliferation; rather, the chromosome abnormality in the myeloid cells appears to mark these elements as the primary aberrations associated with acute myelofibrosis.

- 1248 MELANOSOME AND LYSOSOME: I. LYSOSOMAL ACTIVITY IN RELATION TO GROWTH OF MELANOMA. (E.) Ohtaki, N. (Tokyo Med. Dent. U., Japan). *Bull Tokyo Med Dent Univ* 17(2):89-102, 1970.

An electron microscopic examination was conducted on a Harding-Passey mouse melanoma; lysosomal activity in the tumor, the latency of lysosomal enzymes, and the relationship between lysosomal enzymes and tumor growth were also investigated. Melanoma melanocytes and melanophage cells were observed in the melanomas. Melanoma melanocytes contained mitochondria in abundance, a well-developed endoplasmic reticulum, numerous free ribosomes, and melanosomes. Melanophage cells were similar in appearance to melanoma melanocytes, but they possessed compound melanosomes. Lysosomal enzymes in the melanoma were found in the supernatant, microsomal, and mitochondrial fractions of the tumor homogenate. The heaviest fraction, which sedimented at 700 x g x 10 min, possessed relatively low tyrosinase activity and contained 50% of the succinic dehydrogenase activity. Acid phosphatase activity showed no latency, but cathepsin activity increased with deoxycholate treatment under hypotonic conditions. All enzyme activities increased with increases in tumor wt. However, enzyme activity usually reached peak values at 5-9 days after the commencement of tumor growth, and then declined thereafter. Succinic dehydrogenase activity increased with increases in tumor wt for 21 days before falling off. Tumor wt increased for 29 days, after which necrosis set in.

- 1249 ULCERATIVE COLITIS AND CARCINOMA OF THE BILE DUCTS. (E.) Converse, C. F. (U. Hosp. Cleveland, Ohio), J. W. Reagan and J. J. DeCosse. *Amer J Surg* 121(1):39-45, 1971.

The association of ulcerative colitis and cancer of the bile ducts was investigated in 29 cases and in a survey of cases recorded in the literature. The literature yielded 3,009 cases of chronic ulcerative colitis; in 12 of these patients carcinoma of the bile ducts was also present (0.4%). In the series of 29 cases, 3 of which are described for

the first time, both chronic ulcerative colitis and bile duct cancer occurred in all cases. Most of these patients, were male; average age at onset of symptoms was 25.1 yr (range, 7-59 yr). The severity of ulcerative colitis in bile duct cancer patients was greater than in the usual patient with ulcerative colitis. A nonrandom association appears to exist between ulcerative colitis and bile duct carcinoma; cholangitis often seemed to precede the onset of bile duct carcinoma.

- 1250 B.C.G. AND LEUKAEMIA. (E.) Hems, G. (U. Dept. Soc. Med., Aberdeen, Scotland) and A. Stuart. *Lancet* 1(7691):183, 1971.

The protection from leukemia afforded by childhood vaccination with bacillus Calmette-Guerin (BCG) was investigated in the British population. Vaccination records have been kept since 1954, indicating that BCG vaccination of 13-yr-old children in England and Wales was performed on 7% of these children in 1954, and on 65% by 1967. The incidence of leukemia in these periods was determined, and it was found that leukemia mortality rates have declined in the latter half of the century. By 1970, when 30-60% of the 15 to 19-yr-old population had been vaccinated, the mortality from leukemia had declined from 35×10^{-6} (recorded in 1954 for unvaccinated children) to 24×10^{-6} . While the observed decline in the leukemia mortality rate concurrent with the increasing efficiency of BCG vaccination programs may represent effect and cause, it is also possible that the decline in leukemia mortality was due to other factors.

- 1251 B.C.G. VACCINATION AND LEUKEMIA MORTALITY. (E.) Berkeley, J. S. (Edinburgh). *Lancet* 1(7692):241, 1970.

The effect on leukemia mortality of vaccination with bacillus Calmette-Guerin (BCG) was investigated in 4 Scottish towns. BCG vaccination programs have been in effect in Glasgow since 1954, in Edinburgh and Aberdeen since 1953, and in Dundee since 1955. Leukemia mortality data show that death from leukemia in the 3 age groups 0-4 yr, 5-9 yr, and 10-14 yr increased in Edinburgh, Aberdeen and Dundee, while in Glasgow, the leukemia mortality rate for the 0-4 yr age group more than doubled. Increases in mortality rates were recorded in comparison to mortality data compiled from 1939-1948.

- 1252 CHROMOSOMES AND CAUSATION OF HUMAN CANCER AND LEUKEMIA: VII. THE SIGNIFICANCE OF THE Ph^1 IN CONDITIONS OTHER THAN CML. (E.) Rosselfeld, D. K. (Roswell Park Mem. Inst., Buffalo, N. Y.), T. Han, R. N. Holdsworth and A. A. Sandberg. *Cancer* 27(1):186-192, 1971.

Evidence was found that the Ph^1 chromosome condition is not entirely specific for chronic myelocytic leukemia; 3 cases were examined, 2 of acute myeloblastic leukemia and 1 of chronic erythroleukemia (Di Guglielmo's syndrome) in which the Ph^1 chromo-

some was present. The patients were male of 42-43 yr; in each case the disease was fatal. Chromosome analyses showed Ph^1 -positive cells in bone marrow in 40-100% of the cells examined. The process leading to the development of a Ph^1 chromosome apparently affected the bone marrow cells at or beyond the level of the stem cells. Cases in the literature in which Ph^1 chromosomes were associated with conditions other than chronic myelocytic leukemia were also reviewed.

- 1253 THE ULTRASTRUCTURE OF CARDIAC MYXOMA. (E.) Williams, W. J. (Welsh Natl. Sch. Med., Cardiff), D. Jenkins and D. Erasmus. *Thorax* 25(6):756-761, 1970.

A cardiac myxoma which was excised from the left atrium of a 41-yr-old man was examined by electron microscopy. It appeared as a soft, friable mucoid mass attached by a pedicle to the posterior aspect of the anterior commissure of the mitral valve. Histologically, the myxoma consisted of abundant, amorphous mucoid tissue with scattered single and grouped rounded or stellate cells. The predominant cell type in the myxoma was about 10μ in diameter, of uniform structure, and occurred singly or in tight clusters of 2-4 cells; no giant cells were seen. Nuclei were often irregular in outline; nucleoli and mitotic figures were absent. Numerous Golgi complexes were seen in the cytoplasm; there was a moderate amount of lamellar rough endoplasmic reticulum, and free ribosomes, mitochondria, and glycogen granules. No formed collagen was found, and there was little evidence of pinocytosis. Fine intracytoplasmic fibrils were frequent. Apparently, the myxoma cells were biosynthetically active and were responsible for the production of the stroma cells. The myxoma was thought to be a neoplasm rather than a thrombus.

- 1254 CROWN GALL: AN EXPERIMENTAL MODEL FOR USE IN THE QUANTITATIVE REGULATION OF GENETIC INFORMATION IN THE PRODUCTION OF TUMORS. (Fr.) Guille, E. (Fac. Sci. Orsay, France) and F. Quetier. *Bull Cancer* 57(2):217-238, 1970.

Hybridization of DNA-DNA and RNA-DNA from tumor tissue was studied and compared with those of healthy tissue. The nuclear DNA of crown gall could not be shown to be of bacterial origin; the sedimentation density of DNA of the tumoral tissue was the same as that of healthy tissue. However, it is possible that the bacterial DNA present in the tumor cell was too small a fraction to be detected by the gradient ultracentrifugation method. From experiments of molecular hybridization of DNA and RNA of tumor tissue with nucleic acids of bacterial origin, it appeared that there were sequences common to DNA of tumor tissue and bacterial DNA, and that part of the new sequences had been transcribed into the established tumor tissue. Three types of new sequences existed in the tumor tissue: the sequences common to hybrid DNA and bacterial DNA; the sequences specific to bacterial DNA; and the sequences of hybrid DNA integrated into different loci of the matrix.

The sequences present in tumor tissue were essentially constituted of repetitions of guanylic acid and cytidylic acid. The model for quantitative regulation of genetic information is based on the principal properties of the hybrid DNA which are: hybridization with cytoplasmic ribosomal RNA; its high degree of redundancy; and its desynchronized labeling with respect to the classical nuclear DNA. This model is applicable to the chromomere of higher organisms conceived as a unit of structure and function and to the genetic information of the neoplastic event.

- 1255 ALDOLASE ISOZYME PATTERNS OF REPRESENTATIVE TUMOURS IN THE HUMAN NERVOUS SYSTEM. (E.) Kumanishi, T. (Brain Res. Inst., Niigata U., Japan) and F. Ikuta. *Acta Neuropath* 16(3):220-225, 1970.

The aldolase isozyme activities of human nervous system neoplasms were investigated. Mixed astrocytomas with oligodendroglioma, plump cell type and anaplastic cell type, were shown by thin layer polyacrylamide gel electrophoresis to have high levels of activity of aldolase C in the 5-membered hybrid set of A-C. Malignant gliomas, neuroblastomas, meningiomas, pinealomas, cranio-pharyngioma and pituitary adenomas, on the other hand, showed relatively low levels of aldolase activity, and, in some cases, no appreciable aldolase activity.

- 1256 SPECIFIC CHROMOSOME ANOMALY ASSOCIATED WITH AUTONOMOUS AND CANCEROUS DEVELOPMENT IN MAN. (E.) Muldal, S. (Christie Hosp., Manchester, England), R. Elejalde and P. W. Harvey. *Nature* 229(5279):48-49, 1970.

The over- and under-representation of chromosome types in neoplastic tissues was examined by a computer method which sorted chromosomes according to their centromere indices and their lengths. A total of 60,000 chromosome measurements were made. A significant gain was found in all samples of neoplastic tissue in the chromosomes of centromere index 0.50-0.45 and length 5.97-2.44 μ ; chromosomes in this range averaged 11.73% in neoplastic tissue and 5.54% in normal tissue. Neoplastic tissues showed depressed numbers of chromosomes with centromere indices of 0.16-0.05 and with lengths of 5.97-2.44 μ ; neoplastic tissues showed 3.07% of these chromosomes, and normal tissue, 10.11%. The excess in "chromosome 16" chromosomes in malignant cells apparently was due to iso-chromosomes and translocations, especially the acrocentrics. Such translocations may lead to the loss of normal nucleolar organizers, and it is possible that malignant cells contain D and G translocations which are not known constitutionally, having lost the nucleolar organizer present in normal cells.

- 1257 FUNCTIONAL SEQUENCES MODULATED BY MORPHOLOGICAL TRANSITIONS IN HUMAN LYMPHOID CELLS GROWN *IN VITRO*. (E.) Drewinko, B. (M. D.

Anderson Hosp. Tumor Inst., Houston, Tex.), J. M. Trujillo and C. F. Tessmer. *Science* 171(3967):185-186, 1971.

The morphological changes exhibited by human lymphocytes derived from a patient with lymphoma and cultured for 5 yr were observed. Reticuloid fusiform cells and lymphocytoid and plasmacytoid round cells predominated; binucleate cells and transitional cells were also abundant. Indirect immunofluorescence tests indicated that the cells synthesized gamma globulin. Round cells comprised 80% of fluorescent cells, with fusiform cells making up 10% of fluorescent cells. The median generation time from 1 cell division to the next daughter cell was 36 hr. Most cells underwent changes in shape from round to fusiform and back to a round form. Dividing fusiform cells occasionally gave rise to an elongated and a round daughter cell, more often to 2 fusiform cells. Daughter cells were sometimes seen to fuse and produced a single binucleate cell; the fusion cell then dissociated into a mobile round cell, or it divided to give 4 round daughter cells. Round cells demonstrated marked pyroninophilia and showed intense fluorescence when exposed to fluorescein-labeled antiserum to human gamma globulin, while fusiform cells showed little or no fluorescence. This finding apparently indicates that these cells can only synthesize immunoglobulins when they assume a round shape. It also appeared that human immunoglobulin-producing cells undergo cyclic morphological changes which are expressions of functional differentiation.

- 1258 CAROTID BODY TUMORS: FAMILIAL AND BILATERAL. (E.) Wilson, H. (Dept. Surg. U. Tennessee, Memphis). *Trans South Surg Ass* 81:241-246, 1970.

The diagnosis and treatment of tumors of the carotid body were reviewed with special attention to the familial occurrence of these lesions. Although most carotid body tumors are benign, a few are malignant and spread to contiguous structures and to regional lymph nodes. Carotid tumors occurring in a familial distribution are more likely to be bilateral than isolated carotid tumors. In a newly reported case, a bilateral carotid body tumor was discovered in a 65-yr-old man; 5 of 6 siblings and 3 of their children also have carotid body tumors, 2 of which are bilateral. One brother had no tumor, but his son did.

- 1259 A GANGLIONEUROMA IN THE ADRENAL MEDULLA OF A RAT BEARING A PREOPTIC-ANTERIOR HYPOTHALMIC LESION. (E.) Barofsky, I. (Mass. Coll. Pharm. Boston), E. Matalka and A. B. Russfield. *Cancer Res* 30(12):2913-2916, 1970.

The discovery of a ganglioneuroma in the adrenal medulla of a male rat which had received a unilateral preoptic-anterior hypothalamic lesion at 3 months is reported. The tumor was discovered on autopsy when the rat was 1 yr old. Two well-differentiated components were found: mature ganglion cells and neural

tissue; no normal medullary cells were seen in the tumor. Neural tissue was found in 21 of the 27 other rats with lesions, and in 28 of the 40 intact controls. Ganglion cell differentiation was found in 12 of 27 other rats with lesions, and in 13 of 40 controls. However, none of the other rats developed ganglioneuromas. The stimulus which might lead to ganglion cell differentiation may be a sustained neural stimulation of the adrenal medulla resulting from a pre-optic lesion.

1260 THE CHROMOSOMAL ABERRATION OF DOUBLE-MINUTES IN THREE GLIOMAS. (E.) Mark, J. (Inst. Path. U. Lund, Sweden) and I. Granberg. *Acta Neuropath* 16(3):194-204, 1970.

The chromosomes of about 70 human malignant gliomas were studied, and the clinical and pathological features of 3 tumors with a regular occurrence of double-minutes (small paired chromatid bodies in addition to the ordinary chromosomes) were determined. The double-minutes were extremely small and ranged in number between 1 and 100 per cell. Their occurrence was not related to any specific deviations in the ordinary chromosomes, although the double minutes might be derived from one or more pulverized chromosomes.

1261 MALIGNANT DEGENERATION OF GONADAL DYS-GENESIS. (Ger.) Schaller, A. (2nd U. Women's Clin., Vienna, Austria), P. Fischer and E. Golob. *Geburtsh Frauenheilk* 30(11):980-985, 1970.

A case of gonadal dysgenesis which developed into malignancy is described in an 18-yr-old girl with uterine hypoplasia and amenorrhea. In the course of laboratory tests, no estrogen effect was seen in the vaginal smear, the urine contained no pregnandiol and the histological diagnosis was "undifferentiated" gonadal dysgenesis. The oral mucosal smear showed no sex chromatin, and the chromosomal determination of lymphocyte cultures showed a 46 XY karyotype. The association of the XY constellation with malignancy was confirmed in this case by the development of a tumor within 2 yr of the diagnosis of gonadal dysgenesis, although no tumor growth was detected in the first gonadal streak. Metaphases with normal diploid male chromosomal configuration associated with malignant tumor-specific marker chromosomes were found within the tumor.

1262 FAMILIAL OCCURRENCE OF INTRACRANIAL MENINGIOMA. (Ger.) Grunert, V. (Neurosurg. U. Clin., Vienna, Austria), J. Horcajada and M. Sunder-Plassmann. *Wien Med Wschr* 120(46):807-808, 1970.

A study of 2 male siblings (53 and 49 yr-old) with intracranial meningioma is reported. Both cases were operated on within 11 months of each other, after histological confirmation of the intracranial meningioma. The older brother had a suprasellar meningioma removed completely, and in the other brother a large meningioma was located at the third ventricle and in both lateral ventricles, which could not be completely extirpated. Another member of this family, a sister, also died of a brain tumor, but the type of tumor was not specified. The possibility of a genetic susceptibility to intracranial meningioma is discussed.

1263 THE EARLY RADIOLOGICAL CHANGES IN PULMONARY AND PLEURAL ASBESTOSIS. (E.) Fletcher, D. E. (North Lonsdale Hosp., Barrow-in-Furness, England) and J. R. Edge. *Clin Radiol* 21(4):355-365, 1970.

1264 A BREAST SARCOMA CONTAINING RHABDOMYOSARCOMATOUS AND OTHER METAPLASTIC ELEMENTS. (E.) Bird, C. C. (Dept. Path., U. Aberdeen, Scotland). *J Path* 101(3):286-289, 1970.

1265 TRICHOMONIASIS AND CANCER OF THE UTERINE CERVIX. (Rus.) Barats, A. M. (21st Hosp. Sverdlovsk, USSR). *Sovet Med* 33(10):147, 1970.

1266 CANCER OF THE OTHER BREAST. (Fr.) Menye, P. A. (Dakar, Senegal), D. Simaga and S. Atangane. *Bull Soc Med Afr Noire Lang Franc* 15(1):15-24, 1970.



AUTHOR INDEX

AARONSON, S.A.	1037, 1095	BAEZ, A.G.	1199	BERG, J.W.	0858
ACHESON, E.D.	0982	BAILAR, J.C., III	1181	BERGE, T.	1190*
ADAMSON, R.H.	1204	BAKAY, M.	1045	BERGOLITS, V.M.	1075
AGEYENKO, A.I.	1048, 1050	BALDWIN, R.W.	1132	BERKELEY, J.S.	1251
AJELLO, L.	1153	BANIER, M.W.	1005	BERNARD, C.	1141*
ALFIERI, A.	1128	BARANIKOV, G.A.	0833	BERNARD, P.A.	0851
ALLEN, D.W.	1027	BARAJAS, E.	1193*, 1194*	BERNARD-DEGANI, O.	1141*
ALLISON, A.C.	1113, 1117	BARATS, A.M.	1265*	BHIDE, S.V.	0969, 0970
ALM, G.V.	1134	BARBANTI-BRODANO, G.	1092	BIANCIFIORI, C.	0910
ALTWEIN, J.E.	1186	BARBATANO, L.	1128	BIRD, C.C.	1264*
AMETANI, T.	1018	BARO, D.S.	1125	BISHOP, J.M.	1081, 1088
ANDELMAN, J.B.	0865*	BARKER, B.E.	1143	BISWAL, N.	1076
ANDERSON, C.	1176	BARNARDT, J.H.	0888	BLACK, H.S.	0918
ANDERSON, K.M.	0932	BARNES, J.E.	1013	BLACK, P.H.	1097
ANDERSON, R.E.	1001	BARGFSKY, I.	1259	BLACKLOW, N.R.	1056
ANDERSSON, B.	1007	BARON, S.	0953	BLAKEMORE, W.S.	1116
ANGHILERI, L.J.	1233	BARRON, B.A.	1157	BLASCHECK, J.A.	0925
ANONYMOUS	0861, 1130, 1142*, 1244	BARSKI, G.	0838	BLEANEY, B.	1012
ANTHONY, H.M.	0980	BASHKAYEV, I.S.	1050	BLOCH, K.J.	1097
ANTONELLO, C.	0938	BATES, R.R.	0891, 0931, 0934	BOECKER, B.B.	1013, 1014, 1015
AOKI, T.	1034	BAUER, H.	1064, 1065	BOESENBERG, H.	0881*
ARCOS, J.M.	0956	BAUMANN, K.	0989*	BOIRON, M.	1068
ARIES, V.	1189	BAUSSERMAN, L.L.	0891	BOLLER, K.	0903
ARKHIPOV, G.N.	0947	BEARD, J.W.	1105	BOLOGNESI, D.P.	1064, 1065
ATANGANE, S.	1266*	BECK, E.G.	0936	BONAR, R.A.	1105
AUERBACH, G.	0973, 0974	BELADI, I.	1045	BONNET-GAUDOS, M.	0870*
AUGER, C.	0992	BENDICH, A.	1202	BOQUIST, L.	1246
AUSTIN, B.J.	0918	BENJAMIN, S.A.	1015	BORENFREUND, E.	1202
AXELPOD, D.	1094	BENNINGTON, J.L.	1161	BORNSTEIN, F.P.	1171
AXELSSON, S.	1222	BEN-SIRA, I.	1213	BOSIN, F.R.	0863*
BABA, K.	1044	BENYESH-MELNICK, M.	1060, 1076	BOSMANN, H.B.	1114
BABCHIN, I.S.	0844	BERENBLUM, I.	0893	BOTSMAN, N.E.	0897
BAECHLER, C.A.	1126	BERG, B.	1240	BOUCHAYER, M.	1154

BOULESTEIX, J.
0870*
BRADY, R.O.
1091
BRANDT, L.
1240
BRANTON, P.E.
1106, 1110
BREZAK, M.A.
1199
BRIAND, P.
0854
BRODY, J.I.
1116, 1212
BROOKES, P.
0941
BROWN, D.G.
0994
BROWN, E.
0861
BROWN, E.V.
0924
BRYAN, G.T.
0899
BRYANT, J.I.
1201
BUCK, R.C.
1209
BUCKLEY, C.E., III
1123
BURG, H.E.
0907
BUSBY, W.F., JR.
1205
BUTEL, J.S.
1100
BUTLER, W.H.
0950, 0952
CALAMARI, F.
1184
CAMPADELLI-FIUME, G.
0961
CAMPAIGNE, E.
0863*
CAMPBELL, J.G.
1031
CARDIFF, R.D.
1144
CARLASSARE, F.
0938
CARO, W.
1162
CASE, M.T.
1151
CASPARY, E.A.
1197
CATALANO, L.W.
1061
CEGLOWSKI, W.S.
1022
CEGRELL, L.
1222
CERNY, E.
0922
CESARO, A.N.
0878*

CHAN, G.Y.
1111
CHAN, J.C.
1107, 1111
CHAN, P.C.
0935
CHANEY, S.Q.
1210
CHANG, R.S.
1073
CHANG, S.S.
1070
CHARDOT, C.
1159
CHARNEY, J.
1067
CHAUVEAU, J.
0921
CHEEVERS, W.P.
1106, 1110
CHEN, L.
0928
CHEN, M.M.-S.
1234
CHEPINOGA, O.P.
0972
CHERNOZEMSKI, I.N.
0971
CHERRY, C.P.
0887
CHEUNG, A.S.M.
1234
CHIFFELLE, T.L.
1014, 1015
CHIN, C.T.
0978, 0979
CHIRIGOS, M.A.
1036, 1069
CHOUROULINKOV, I.
0926
CHRIST, M.L.
1239
CIKES, M.
1077
CLARK, H.F.
0937
CLEMMESSEN, J.
0868*
CLIFFORD, W.
1024
COHEN, D.
1183
COHEN, S.
1126
COLE, P.
0976, 1187
COLLINS, J.J.
1097
CONNEY, A.H.
0939
CONSIGLI, R.A.
1112
CONVERSE, C.F.
1249
COOPER, E.H.
1236

CRADDOCK, V.M.
0831
CRAIG, A.W.
0949
CRAIG, P.S.
1174
CROIZAT, H.
1011
CROSSEN, P.E.
1206
CROSSWHITE, L.H.
1235
CROWTHER, J.S.
1189
CRUMPACKER, C.S.
1052
CUMMING, R.B.
0902
CUNNINGHAM, M.P.
1140
DALLENBACH-HELLWEG, G.
1160
DANIEL, M.D.
1057, 1059
DAVIES, D.A.L.
1141*
DE CARNERI, I.
1238
DE CHOLNOKY, T.
0986*
DECLOITRE, F.
0923
DE COSSE, J.J.
1249
DE ESTABLE-PUIG, J.F.
0992
DE ESTABLE-PUIG, R.F.
0992
DEFENDI, V.
1089
DEHNEN, W.
0936
DE KOCK, D.H.
0888
DELALIEUX, G.
1223
DERINGER, M.K.
1198
DEWYS, W.
1232
DIAMOND, L.
0937
DIETZ, W.
0965
DIPPLE, A.
0933
DI RE, F.
1238
DMITRIEV, V.N.
1145
DOERFLER, W.
1051
DOI, T.
1028, 1030, 1063
DOLIN, R.
1056

DONALDSON, W.E.
 0916
 DOUGHERTY, T.F.
 1003
 DOUGHTY, W.E.
 1001
 DOWDLE, W.R.
 1054
 DRAPER, G.J.
 1180
 DRASAR, B.S.
 1189
 DREWINKO, B.
 1257
 DRUCKREY, H.
 0905
 DUESBERG, P.H.
 1066
 DULBECCO, R.
 1109
 DULLY, M.
 1247
 DUNCAN, M.E.
 0941
 DUPLAN, J.F.
 0999
 DUPLANTIER, D.P.
 0896
 DURR, F.E.
 1023
 EATON, S. DEL A.
 0931
 ECKHARDT, W.
 1109
 EDGE, J.R.
 1263*
 EDGINGTON, D.N.
 1006
 EISENBRAND, J.
 0989*
 ELEJALDE, R.
 1256
 ELGJO, K.
 1208, 1216
 EMBLETON, M.J.
 1132
 ERASMUS, D.
 1253
 ESCHENBACH, C.
 1041
 EVANS, V.J.
 1200
 EZDINLI, E.Z.
 1235
 FABIANI, A.
 0963, 0964
 FAHR, K.
 0988*
 FAIRLEY, G.H.
 1129
 FAN, K.
 1124
 FANSHIER, L.
 1081, 1088
 FAUMENI, J.S., JR.
 1181

FECHNER, R.E.
 0984
 FEDEROVSKAYA, M.I.
 0943
 FELDMAN, D.G.
 1039
 FENNER, F.
 0864*
 FIALKOW, P.J.
 1201
 FIEL, R.J.
 1032
 FIELD, E.J.
 1197
 FINLAYSON, A.
 1170
 FINLEY, A.G.
 1206
 FISCHER, P.
 1261
 FIUME, L.
 0961
 FLETCHER, D.E.
 1263*
 FOERSTER, C.
 1041
 FONG, C.K.Y.
 1099
 FONTAINE, J.L.
 0870*
 FOUTS, J.R.
 0848
 FRANKS, L.M.
 1229
 FRASER, C.E.O.
 1059
 FREEDMAN, M.H.
 1237
 FREEMAN, A.E.
 0953
 FREIENSTEIN, C.
 0892
 FREIENSTEIN, S.
 0892
 FREMIOTTI, A.
 1128
 FRETZIN, D.F.
 1239
 FRIEDEL, G.H.
 0976
 FRIEDMAN, H.
 1022
 FRINDEL, E.
 1011
 FRITSCH, R.S.
 1040
 FUCCILLO, D.A.
 1061
 FUJII, K.
 0958
 FURUKAWA, T.
 1121
 GABUTTI, V.
 0676*
 GADOMSKA, H.
 1192*

GAILLARD, J.
 0851, 1154
 GALLO, R.C.
 1204
 GAMBURG, V.P.
 1042
 GANGAL, S.G.
 1072, 1120
 GANTT, R.
 1200
 GARAPIN, A.C.
 1061
 GARCIA, F.G.
 1059
 GARDELL, C.
 0925
 GARDNER, M.B.
 1182
 GARFINKEL, L.
 0973, 0974
 GARISOAIN, M.J.
 0956
 GAVOSTO, F.
 0676*
 GENTIL, A.
 0926
 GHELELOVITCH, S.
 0998
 GIBSON, A.A.M.
 1170
 GIBSON, W.
 1069
 GILCHRIST, G.H.
 1237
 GILDEN, R.V.
 1070
 GIMMY, J.
 0905
 GINER, J.
 0871*
 GLOVER, D.J.
 0940
 GLUCKSMANN, A.
 0887
 GODARD, C.
 1068
 GOLDBERG, G.M.
 1168
 GOLDE, A.
 1078
 GOLDEN, H.D.
 1073
 GOLIGHER, J.C.
 1156
 GOLOP, E.
 1261
 GORBACH, P.D.
 1180
 GORBANE, G.P.
 0897
 GOSS, S.G.
 0836
 GOTHOSKAR, S.V.
 0969
 GRADY, L.
 1094

GRAHAM, C.
 1061
 GRAHAM, C.E.
 1158
 GRANBERG, I.
 1260
 GRANBOULAN, N.
 1203
 GREY, H.M.
 1127
 GRIMES, W.J.
 1101
 GROETENBRIEL, C.
 0981
 GRONMARK, T.
 1164*
 GROSS, L.
 1039
 GROSS, M.
 1168
 GROSSI-PAOLETTI, E.
 0963, 0964
 GRUENSTEIN, M.
 0908
 GRUENTHAL, D.
 0959
 GRUNERT, V.
 1262
 GRUNNET, M.L.
 1196
 GUILLE, E.
 1254
 GUILLEMAIN, B.
 1068
 GUMBANN, M.R.
 0919
 GUNVEN, P.
 1024
 GUNZ, F.W.
 1206
 GUSSARSKY, J.
 1168
 GYSELEN, A.
 0872*
 HABIBI, A.
 1179
 HADFIELD, E.H.
 0982
 HAGUENAUER, J.P.
 0851, 1154
 HAKOMORI, S.
 1102
 HALL, J.G.
 0940
 HALL, W.T.
 1067
 HALPERN, B.C.
 1210
 HALPERN, R.M.
 1210
 HAMILTON, P.B.
 0916
 HAMMARSTROM, L.
 1016*
 HAMMOND, E.C.
 0973, 0974

HAMMOND, G.D.
 1237
 HAN, T.
 1252
 HANAFUSA, H.
 1086
 HANAFUSA, T.
 1086
 HANES, B.
 1182
 HANING, H.
 0976
 HARD, G.C.
 0950, 0952
 HARE, J.D.
 1107
 HAREL, J.
 1026
 HARRIS, R.
 1141*
 HARROLD, B.
 1073
 HARTLEY, J.W.
 1115*
 HARTVEIT, F.
 1122
 HARTZELL, R.W.
 1046
 HARVEY, P.W.
 1256
 HATAKEYAMA, S.
 0925
 HAWKSWORTH, G.
 1189
 HAYS, E.F.
 1035
 HEATH, C.W.
 1123
 HEIDBREDER, G.
 1182
 HEILMANN, H.P.
 0995
 HELE, P.
 1205
 HELLENBROICH, D.O.
 0959
 HEMS, G.
 1250
 HENDERSON, J.W.
 1149
 HENLE, G.
 1024, 1025
 HENLE, W.
 1024, 1025
 HENNINGS, H.
 1216
 HENZELL, S.
 1229
 HERMANUTZ, D.
 1010
 HERNANDEZ, F.
 0960
 HERRANEN, A.
 1219
 HERRERA, F.
 1204

HERZBERG, M.
 1103
 HESTON, W.E.
 1067
 HEUSON, J.C.
 0930, 1243
 HIERHOLZER, J.C.
 1054
 HILL, M.J.
 1189
 HILLSTROM, L.
 0997
 HINUMA, Y.
 1020
 HIRONO, I.
 0895
 HIRSHAUT, Y.
 1023
 HO, J.K.
 1111
 HOAGLAND, H.C.
 1147
 HOBBS, C.H.
 1013, 1014, 1015
 HOFFMANN, D.
 0977
 HOGGAN, M.D.
 1056
 HOLDSWORTH, R.N.
 1252
 HOLLAND, J.M.
 0885
 HOLSMAN, J.
 0961
 HOLSTO, L.R.
 1002
 HONDA, Y.
 1202
 HOPKINS, M.S.
 1099
 HORCAJADA, J.
 1262
 HOSSFELD, D.K.
 1235, 1252
 HOWARD, R.J.
 0882*
 HOWARTH, J.L.
 1001
 HUANG, L.H.
 1234
 HUANG, S.N.
 1118
 HUEBNER, R.J.
 1034, 1070, 1182
 HUNG, P.
 1085
 HUNT, R.D.
 1059
 IKUTA, F.
 1255
 IMBENOTTE, J.
 1026
 INGALLS, T.H.
 1219
 IRLIN, I.S.
 1038

ISBRANDT, R.
 0924
 ISHIBASHI, Y.
 1231
 ISHIDA, K.
 1172
 ITO, Y.
 1074
 IVANKOVIC, S.
 0905
 IVANOV, I.I.
 0852
 IWA, N.
 1030
 JACKSON, J.
 1088
 JACKSON, J.L.
 1143
 JANISCH, W.
 0965
 JAO, W.
 1239
 JEE, W.S.S.
 1003
 JENKINS, D.
 1253
 JENSEN, M.K.
 1146
 JOHANSSON, B.
 1025
 JOHNSON, D.F.
 0994
 JONES, R.K.
 1013, 1014, 1015
 JUSSAWALLA, D.J.
 1177
 KADACH, D.
 1135
 KAESER, H.
 1242
 KAMBOJ, V.P.
 0889
 KAMINSKAYA, L.P.
 0943
 KANAPILLY, G.M.
 1013
 KANPFSKY, P.
 1221
 KAR, A.B.
 0889, 0985
 KAREWICZ, Z.
 1192*
 KARKUN, J.N.
 0985
 KARSTEN, C.
 0904
 KASILI, E.G.
 1166
 KASPER, C.B.
 0913
 KATAGIRI, S.
 1020
 KATO, H.
 1172
 KATO, R.
 0967

KATO, S.
 1028, 1029, 1030,
 1063
 KAWAKAMI, H.
 1087
 KEENEY, A.H.
 1234
 KEITH, L.
 0861
 KELLEN, J.A.
 0932
 KEOWN, D.
 1211
 KEVIN, D.M.
 0860
 KHOLMUKHAMEDOVA, N.M.
 1048
 KING, D.R.
 1143
 KING, R.J.B.
 0834
 KINT, A.
 0862*
 KINZEL, V.
 0892
 KIPLING, M.D.
 0859
 KIRIMOTO, K.
 1217
 KIRMAN, D.
 0973, 0974
 KIRSCH, M.
 0936
 KIRSTEN, W.H.
 1108
 KIRZEDER, H.
 0966
 KISELEV, F.L.
 1038
 KIVILAAKSO, E.
 0901
 KLEHR, H.U.
 1231
 KLEIN, G.
 0841, 1024, 1025,
 1121
 KLINGMULLER, G.
 1231
 KMET, J.
 0857
 KNAPP, D.R.
 0863*
 KNEDEL, M.
 0966
 KNORRE, D.
 0898
 KOBAYASHI, N.
 1121
 KOGAN, B.
 1182
 KOGAN, I.YA.
 1048
 KOLEV, K.
 0996
 KOLODZIEJSKA, H.
 1167

KONOBE, T.
 1029
 KOPROWSKI, H.
 1092
 KOROSTELEVA, T.A.
 0911
 KOSZAROWSKI, T.
 1192*
 KOVACS, K.
 0925
 KRAIN, L.S.
 1178
 KRAWCZYNSKI, K.
 1034
 KREIBICH, G.
 0892
 KREN, V.
 0900
 KRENOVA, D.
 0900
 KRIPKE, M.L.
 0894
 KRISHNA MURTHY, A.S.
 1199
 KRUEGER, C.
 0904
 KRUSE, H.
 0905
 KUBINSKI, H.
 0913
 KUCHERIA, K.
 1230
 KUEHNEL, W.
 1041
 KUMANISHI, T.
 1255
 KUNKEL, H.G.
 1127
 KURTH, R.
 0856
 KUWATA, T.
 0867*, 1087
 LACHAPPELLE, F.L.
 1243
 LACOUR, F.
 1026
 LAFONT, J.
 0991*
 LAFONT, P.
 0991*
 LAGEMAN, A.
 0965
 LANDSCHUTZ, C.
 0905
 LANGLOIS, A.J.
 1105
 LANGMAN, M.J.S.
 1228
 LARSSON, B.
 1007
 LASNE, C.
 0926
 LAUMOND, J.
 1068
 LAURENCE, K.R.
 1208

LE BRETON, E.
0849
LEDERER, J.
0879*
LEDLIE, E.M.
1180
LEE, A.E.
1215, 1226
LEE, A.K.Y.
1119
LEE, C.G.
1049
LEE, J.A.H.
0835
LEE, K.W.

0978, 0979
LEE, P.N.
1191*
LEE, K.O.
1211
LEGROS, N.
0930, 1243
LEHMAN, J.M.
1089
LEHNER, T.
1150
LEKSELL, L.
1007
LEONE, G.
0877*
LEVIN, A.G.
1140
LEVIN, M.J.
1052
LEVINSON, W.
1081
LEVINSON, W.E.
1088
LEVY-PINTO, S.
1188
LEWIS, A.M., JR.
1052
LEWIS, R.
1060
LINDSTROM, F.D.
1139
LINMAN, J.W.
1147
LIONS, J.
1214
LIU, W.
1225
LONAI, V.
0893
LONDON, W.T.
1061
LOOS, J.A.
1137
LOOSLI, C.G.
1182
LOTLIKAR, P.D.
0908, 0909
LOWE, C.R.
1187
LUCAS, H.F., JR.
1006

LUDWIG, G.
1041
LUEDERS, G.
1227
LUNDBERG, S.
1190*
MAASS, H.
0959
MACBETH, R.G.
0982
MAC DONALD, J.B.
1228
MACKAY, B.
1161
MACKAY, I.R.
1119
MAC MAHON, B.
1187
MAGEE, P.N.
0954, 0961
MAGILNER, L.
1221
MAIR, A.
1170
MAIR, W.
1007
MAISIN, J.R.
1009
MAKAVEEVA, V.
0852
MAKINO, S.
1224
MALAVIYA, B.
0985
MALLING, H.V.
0855
MANASTER, J.
1223
MANOJLOVIC, N.
0936
MARK, J.
1084, 1260
MARKUN, F.
1006
MARSHALL, K.G.
1118
MARTIN, M.A.
1090, 1095
MARTINEZ DE MORENTIN, J.
0960
MARTINEZ-MANAUTAU, J.
0871*
MARYLANDER, H.
1182
MASERA, P.
0876*
MASSICOT, J.
1036
MATALKA, E.
1259
MATSUBARA, S.
1008
MATSUYA, Y.
1241
MAUDERLY, J.L.
1013

MAYS, C.W.
1000, 1003
MC ADAM, W.A.F.
1156
MC CLELLAN, R.O.
1013, 1014, 1015
MC DONNELL, J.P.
1081
MC EWEN, J.
1170
MC FARLANE, E.S.
1049
MC FEE, A.F.
1005
MC GREGOR, D.H.
1172
MC KINNELL, R.G.
0896
MC LEAN, A.E.M.
0954
MEITES, J.
0929
MELENDEZ, L.V.
1057, 1059
MELLOR, J.E.
1206
MELLORS, R.C.
1034
MENYE, P.A.
1266*
MERGENHAGEN, S.E.
0882*
MERRILL, J.M.
0835
MEUNIER, M.
0921, 0923
MIKUNI, C.
1224
MILLER, D.G.
1140
MILLER, G.
1021
MILLER, M.H.
1021
MINEKAWA, Y.
1044
MIRRA, A.P.
1187
MISFELDT, D.S.
1144
MISHIMA, Y.

0846
MISTRY, P.B.
0999
MITELMAN, F.
1084
MIYAMOTO, T.
1086
MOBARAK, M.A.
1212
MOBBS, B.G.
0890
MODAN, B.
1175
MOHIT, B.
1124

MOISE, G.
 0983
 MONNOT, P.
 0999
 MONROE, J.H.
 1023
 MONSON, R.R.
 0976
 MONTAGNIER, L.
 1079
 MONTI, A.
 0993
 MOORE, D.H.
 0837, 1067
 MORA, P.T.
 1091
 MOREL, C.
 1203
 MORGAN, D.L.
 0931
 MORI, Y.
 1029, 1030
 MORRIS, V.L.
 1058
 MORTENSEN, E.
 1220
 MOSKOVKINA, O.YA.
 1075
 MOUNIER-KUHN, P.
 0851
 MUCCI, I.
 1045
 MUELLER, R.
 1010
 MULDAL, S.
 1256
 MUNSON, B.R.
 1032
 MUTO, T.
 1155
 NYNORS, L.S.
 1180
 NACHTIGAL, M.
 1100
 NAGASAWA, H.
 0927, 1207
 NAHMIAS, A.J.
 1061
 NAITO, M.
 1028, 1029, 1030,
 1063
 NAKAO, K.
 1138
 NEBERT, D.W.
 0891
 NEGRONI, G.
 1104
 NEIMAN, P.E.
 1201
 NEISS, E.S.
 0863*
 NEURATH, A.R.
 1046
 NEWBERNE, P.M.
 0915
 NGAMWATANA, W.
 0967

NIALI, H.D.
 1027
 NICHOLS, W.W.
 0866*
 NILSSON, A.
 1016*
 NISKANEN, E.
 0901
 NORDLING, S.
 1002
 NOTKINS, A.L.
 0882*
 NOWINSKI, R.C.
 0837
 OBARA, Y.
 1224
 ODA, T.
 1080, 1098
 ODILI, J.L.
 1131
 OEHLERT, W.
 0845
 OHMORI, S.
 1017
 OHTAKI, N.
 1248
 OKAMOTO, T.
 1017
 OLD, L.J.
 0837
 OLEFFE, J.
 0981
 OMORI, Y.
 0967
 OMURA, S.
 1098
 ONO, K.
 1028, 1029, 1030,
 1063
 ONO, T.
 1138
 ONODA, T.
 1029, 1030
 OOTA, K.
 1155
 OSSWALD, H.
 0906
 OXFORD, J.S.
 1055
 OYASU, R.
 0907
 OZKAN, A.U.
 0987*
 PAMUKCU, A.M.
 0899
 PAOLETTI, P.
 0963, 0964
 PAPOUSEK, F.
 0922
 PARACHE, R.M.
 1159
 PARK, S.K.
 1116
 PARNES, V.A.
 0860

PARR, I.B.
 1033
 PARSHAD, R.
 1143
 PATTERSON, D.S.P.
 0917
 PAULSCH, W.E.
 0990*
 PECKHAM, M.J.
 1236
 PENN, G.M.
 1127
 PENN, I.
 0839
 PEPPERS, E.V.
 1143
 PETTERSON, U.
 1043
 PHILIP, P.
 1146
 PICKRELL, J.A.
 1013, 1014, 1015
 PIERRE, R.V.
 1147
 PIESENS, W.F.
 0840, 1243
 PIKE, G.Z.
 1114
 PILCH, Y.H.
 1125
 PONTEN, J.
 1082
 PORIES, W.J.
 1232
 POSTE, G.
 1019
 POTOLSKY, A.I.
 1123
 POTOP, I.
 0842
 POTTER, C.W.
 1055
 PRATESI, G.
 1128
 PREHN, R.T.
 0942
 PREUSSMANN, R.
 0905
 PRICE, J.M.
 0899
 PRIGIONE, L.
 1184
 PRINZ, L.M.
 1239
 PRITZKER, K.P.H.
 1118
 PUGH, W.E.
 1115*
 PUSZTAIL, R.
 1045
 QUETIER, F.
 1254
 QUINN, C.E.
 1200
 QUINTRELL, N.
 1081, 1088

RABES, H.
0957
RABINOVITZ, Z.
0951
RAU, H.G.
0920
RALPH, D.D.
1065
RAMMING, K.P.
1125
RAN, M.
1133
RANADIVE, K.J.
1072, 1120
RANDS, E.
1037
RAPOPORT, I.A.
0860
RAPPAPORT, H.
1148
RASKA, K., JR.
1047
RAUSCHKOLB, E.W.
0918
RAVHIAR, B.
1187
RAVICH, R.B.M.
1206
REAGAN, J.W.
1249
REDMAN, H.C.
1014, 1015
REIF, J.S.
1183
REINHARD, M.
1227
REUBER, M.D.
0944, 0945
REXED, B.
1007
RHEE, S.U.
1174
RICHART, R.M.
1157
RICHTER, M.C.
1232
RILEY, F.C.
1149
ROBERT, P.K.
1163*
ROBERTS, B.A.
0917
ROBERTS, G.H.
1004
ROBINSON, H.L.
1085
ROBINSON, W.S.
1085
ROGERS, A.E.
0915
ROIZMAN, B.
1058, 1062
ROM, W.
1160
ROMANOV, V.I.
0886

ROOS, D.
1137
ROSENGREN, A.M.
1222
ROSVOLL, R.V.
1173
ROTH, L.
0983
ROWE, W.P.
1052, 1115*
ROWLANDS, D.T., JR.
1123
ROWLEY, M.
1119
ROWSON, K.E.K.
1033
RUBENCHIK, B.L.
0897
RUBIN, B.A.
1046
RUSSFIELD, A.B.
1259
RYTOEMAA, T.
0901
SACHS, L.
0951
SAENGER, P.
0959
SAIRENJI, T.
1020
SAKNYN, A.V.
1185
SAKSELA, E.
0875*, 1002
SALBER, E.J.
1187
SALZMAN, L.A.
1071
SAN, R.H.C.
0968
SANDBERG, A.A.
1235, 1252
SANFORD, K.K.
1143
SAPRIN, A.N.
1048
SARKAR, N.H.
0837
SASAKI, M.
1224
SASAKI, M.S.
1008
SATO, C.
1136
SATO, H.
0958
SAUER, R.
1027
SCAIFE, J.F.
0914
SCHAFFER, P.
1060
SCHALLER, A.
1261
SCHERF, H.R.
0904

SCHERKER, K.
1203
SCHIFFER, D.
0963, 0964
SCHLEDE, E.
0939
SCHLICE, W.
1227
SCHMIDL, D.
0906
SCHMID, W.
0903
SCHMIDT, F.
0880*
SCHMIDT-BAUMLER, J.
0988*
SCHMITTER, R.
1023
SCHOENBERG, B.S.
1161
SCHULZE, P.
0957
SCHREIBER, D.
0965
SCHROEDER, T.M.
0856
SCHULLER, P.L.
0990*
SCHWARKZ, L.H.
0884
SCOLNICK, E.
1037
SCORRETTI, L.
1153
SEEL, D.J.
1174
SEMENOVA, L.A.
1038
SERBAN, V.
0983
SERY, T.W.
1234
SEVER, J.L.
1061
SHABYNINA, N.K.
1185
SHANI, M.
1175
SHANKARAN, P.
0920
SHANKARAN, R.
0920
SHANMUGARATNAM, K.
1165
SHARON, Z.
1175
SHATALOVA, G.G.
1038
SHCHERBAKOVA, O.E.
1042
SHEBA, C.
1175
SHEININ, R.
1106, 1110
SHERRILL, M.N.
1005

SHIBUYA, C.
0895
SHIDOY, T.
1219
SHIRAI, T.
1034
SIMAGA, D.
1266*
SKATKOV, M.E.
0886
SKOGLUND, R.W.
1161
SLADE, T.A.
0933
SMALL, E.
1151
SMITH, J.A.
0834
SMITH, J.D.
0918
SMITH, R.A.
1210
SMITHERS, D.W.
1218
SMOLER, J.
1188
SOCQUET, M.
1223
SOSKIND, L.
0884
SOURANDER, P.
1007
SOUTHAM, C.M.
1140
SPEAR, P.G.
1062
SPIESS, H.
1000
SPOHR, G.
1203
STARK, O.
0900
STAVROUS, D.
0966
STEERS, A.K.
1140
STEFANI, S.
0993
STEGGLES, A.W.
0834
STEINGLASS, M.
1202
STENMAN, S.
1002
STICH, H.F.
0968
STITT, D.
1021
STOLOFF, I.L.
1221
STONE, L.B.
1096
STRAIN, W.H.
1232
STROHL, W.A.
1047

STRUM, S.B.
1148
STRYCKMANS, P.
1223
STUART, A.
1250
STULBERG, C.S.
1126
SUERE, J.T.
0975
SUESS, M.J.
0865*
SUESS, R.
0892
SUGAR, J.
1152
SUGIMOTO, A.
1217
SULLIVAN, D.
1088
SUMIE, H.
0907
SUNDER-PLASSMANN, M.
1262
SURJAN, M.
0843
SVERAK, L.
1105
SVET-MOLDASKY, G.YA.
1042
SWANBECK, G.
0997
SWETLY, P.
1092
TAHARA, E.
1172
TAKAHASHI, A.
0967
TAKAHASHI, M.
1044
TAKEMOTO, K.K.
1090, 1096
TAKEUCHI, J.
1018
TAKKAR, G.L.
0889
TALWALKAR, G.V.
0969
TANABE, S.
1028, 1063
TANAKA, T.
0949
TANI, E.
1018
TAYLOR, G.
1131
TAYLOR, G.N.
1003
TAYLOR, J.R.
1166
TERAYAMA, H.
1138
TER-GRIGOROV, V.S.
1075
TERRACINI, B.
0962

TESSMER, C.F.
1257
TESTA, M.C.
0962
THEOLOGIDES, A.
1139
THOMAS, E.D.
1201
THOMAS, G.M.
0980
THZOLOV, C.
0996
TICHO, U.
1213
TILLY, R.
1104
TIMOFEYEV, V.T.
1048, 1050
TLOLKA-PLUSZCZYK, J.
0946
TODARO, G.J.
1037
TODD, R.
1141*
TOKUDA, S.
1001
TOMINGAS, R.
0936
TOMOMURA, A.
1008
TOOLAN, H.W.
1099
TORPIER, G.
1079
TRAUL, K.A.
1023
TRILLING, D.
1094
TRUJILLO, J.M.
1257
TUBIANA, M.
1011
TUNG, H.T.
0916
TURCANU, P.
0983
TURNER, W.
1069
TYE, C.Y.
1165
UHLENDORF, C.P.
0953
UMANSKY, Y.A.
0943
VALAORAS, V.G.
1187
VANDENDRIESSCHE, R.
0873*
VANDEPUTTE, M.
0883*
VAN GANSE, W.
0981
VAN SLYCK, E.J.
1247
VARDOSANIDZE, E.SH.
1050
VARICH, N.A.

1038
 VARROY, A.
 1159
 VAUGHAN, J.
 1012
 VELAZQUEZ, G.
 1188
 VENKITASUBRAMANIAN, T.A.
 0920
 VERGER, C.
 1026
 VERHULSDONK, C.A.H.
 0990*
 VERNEKAR, S.D.
 1072, 1120
 VETROVA, E.P.
 0943
 VICENTE, J.
 0869*
 VINCENT, P.C.
 1206
 VISFELDT, J.
 1220
 VIVAR, G.
 1188
 VIZA, D.
 1141*
 VLAHAKIS, G.
 1067
 VLASOV, N.N.
 0948
 VOGT, P.K.
 1066
 VOLFSON, N.I.
 0853
 VONKA, V.
 1060
 VREDEVOE, D.L.
 1035
 WAELBROECK-VAN GAVER, C.
 0930
 WAGNER, E.K.
 1058
 WAGNER, H.P.
 1242
 WAGNER, K.H.
 0912
 WAGNER-HERING, E.
 0912
 WAISSBLUTH, J.G.
 1228
 WALDENSTROEM, J.
 0832
 WALLACE, H.A.
 1116
 WALLER, J.M.

1108
 WALTON, M.F.
 0902
 WARWICK, G.P.
 0971
 WASSERMAN, M.B.
 0909
 WATRACH, A.M.
 1151
 WEINER, L.M.
 1126
 WEISS, D.W.
 0894
 WEISS, L.
 1247
 WEISS, R.
 1083
 WELLINGS, S.R.
 1144
 WELSCH, C.W.
 0929
 WENNERSTRAND, J.
 1007
 WERTHAMER, S.
 0884
 WESSELEN, T.
 1093
 WESTBURY, G.
 0847
 WESTFALL, B.B.
 1143
 WEWER, B.
 0874*
 WHITE, W.L.
 1071
 WIENER, F.P.
 1046
 WIESE, W.H.
 1052
 WILLIAMS, A.O.
 0955
 WILLIAMS, J.F.
 1053
 WILLIAMS, R.C., JR.
 1139
 WILLIAMS, R.E.O.
 1189
 WILLIAMS, S.N.
 0919
 WILLIAMS, W.J.
 1253
 WILLIAMSON, M.E.
 1059
 WILSON, H.
 1258
 WINOCOUR, E.

1103
 WINSHIP, T.
 1173
 WINTERS, A.L.
 1112
 WITZ, I.P.
 1133
 WONG, Y.C.
 1209
 WOODE, G.N.
 1031
 WOODS, M.W.
 1143
 WOODS, W.A.
 1036
 WOOLF, C.R.
 0975
 WYNDER, E.L.
 0850, 0935, 0977
 WYNDHAM, N.
 1245
 YABE, Y.
 1017
 YALCINER, S.
 0899
 YAMAGUCHI, J.
 1020
 YAMAMOTO, G.
 1080
 YAMAMOTO, S.
 1098
 YAMAMOTO, T.
 1172
 YAMANE, I.
 1241
 YANAGISAWA, M.
 1121
 YANAI, R.
 0927, 1207
 YATA, J.
 1121
 YEGHIAYAN, E.
 0925
 YOUNKERS, P.E.
 0953
 YUASA, S.
 1187
 YUSPA, S.H.
 0931, 0934
 ZADOROZHNYA, N.A.
 0972
 ZALDIVAR, R.
 1169
 ZASYPKA, A.T.
 0911
 ZIMMERMAN, J.E., JR.
 1047
 ZUCKERMANN, C.
 1195*

SUBJECT INDEX

- 2-ACETAMIDOFLUORENE
 - BILE DUCT LIGATION, N-HYDROXY-2-ACETAMIDOFLUORENE, ADRENALECTOMY (0908)
- N-ACETOXYACETAMIDOFLUORENE
 - 2-(N-HYDROXY)ACETAMIDOFLUORENE, PHOSPHATE ESTER, ULTIMATE CARCINOGEN (0909)
- 2-ACETYLAMINOFLUORENE
 - DIETARY INDOLE, URINARY BLADDER TUMORS (0907)
- ACTINOMYCIN D
 - MAMMARY TUMOR SUPPRESSION, 7,12-DIMETHYLBENZ(A)ANTHRACENE (0932)
- ADRENAL GLAND
 - ADRENALECTOMY, BILE DUCT LIGATION, N-HYDROXY-2-ACETAMIDOFLUORENE (0908)
 - CORTEX, LIPID HYPERPLASIA, ANILINE, RAT (0925)
 - CORTICAL CARCINOMA, ESTRADIOL, RAT (0890)
 - MEDULLA, PREOPTIC-ANTERIOR HYPOTHALAMIC LESION, GANGLIONEUROMA, RAT (1259)
 - POSTCASTRATIONAL ADRENAL TUMORS, STRAIN VARIABILITY, MICE (1199)
- AFLATOXIN
 - ACID PHOSPHATASE, LYSOSOMAL ENZYME ACTIVITY, CHICKEN (0916)
 - ANALYTICAL METHODS, REVIEW (0881)*
 - B1, B2, G1, G2, ANIMAL FEEDS (0991)*
 - B1, LABELED ACETATE INCORPORATION, HUMAN SKIN LIPIDS (0918)
 - B1, LIVER NUCLEIC ACID SYNTHESIS, PHENOBARBITAL (0919)
 - B1, RNA SYNTHESIS, LIVER CELLS (0914)
 - B1, TWO DIMENSIONAL THIN LAYER CHROMATOGRAPHY, FOOD PRODUCTS, PEANUTS (0990)*
 - LIPOTROPE-DEFICIENT DIET, LIVER TUMORS (0915)
 - LIVER, ENZYME ACTIVITY, CITRIC ACID CYCLE (0920)
 - METABOLISM IN LIVER, DEGRADATION PRODUCTS (0917)
- AGE
 - DISTRIBUTION, HODGKIN'S DISEASE (1218)
 - TUMORIGENICITY OF MOUSE CELL LINES, IN VITRO NEOPLASTIC TRANSFORMATION (1229)
- AIR POLLUTION
 - URBAN, CARCINOMA OF THE TONSIL, CANINE RESPIRATORY TRACT CARCINOMA (1183)
- ALKYLATING AGENT
 - CYCLOPHOSPHAMIDE, CARCINOGENICITY, RAT, MOUSE (0906)
 - 1,3-PROPANE SULFONE, 1,4-BUTANE SULFONE, RATS, NEUROGENIC TUMORS (0905)
 - TRENIMON, MUTAGENESIS, HAMSTERS, BONE MARROW (0903)
- AMINOACETONITRILE
 - METABOLISM, DIMETHYLNITROSAMINE (0961)
- AMINO ACID
 - ARGININE DEPRIVATION, POLYOMA VIRUS, INFECTION (1112)
 - LEUKOSIS, ANTIGEN, VIRUS (1027)
- AMP
 - CELL SURFACE ALTERATIONS, ROUS VIRUS, POLYOMA VIRUS (1079)
- ANILINE
 - LIPID HYPERPLASIA, RAT ADRENAL CORTEX (0925)
- ANTIBODY
 - GROSS LEUKEMIA VIRUS, GLOMERULONEPHRITIS, MOUSE (1034)
 - GROSS LEUKEMIA VIRUS, IMMUNO-FLUORESCENT FOCUS ASSAY (1036)
 - PRODUCTION, CANCER PATIENTS, 17D YELLOW FEVER VIRUS VACCINE (1140)
 - TITERS, SURVIVAL TIME, CANCER PATIENTS, FLAGELLIN (1119)
 - TITERS IN HODGKIN'S DISEASE, EPSTEIN-BARR VIRUS (1025)
 - VIRUS, HUMAN SERA, EPSTEIN-BARR, HERPES (1063)
- ANTIGEN
 - AMINO ACID, LEUKOSIS, VIRUS (1027)
 - CANCER TEST, BASIC PROTEIN, LYMPHOCYTE SENSITIZATION (1197)
 - DEN-86, HEPATOMA, DIETHYLNITROSAMINE, RAT (0956)
 - EPSTEIN-BARR, CLONED HUMAN LEUCOCYTES (1021)
 - LEUKEMIA, ISOLATION, MAN (1141)*
 - LEUKEMIA, LYMPHOMA, THYMUS-LYMPHOID TISSUE (1121)
 - MELANOMA, ACUTE LEUKEMIA, HUMAN (1129)
 - POLYPEPTIDE, AVIAN MYELOBLASTOSIS VIRUS (1065)
 - PROTEIN SYNTHESIS, MYELOMA CELL-LYMPHOMA CELL HYBRID (1124)
 - RESPONSE, DEFECTIVE VIRUS, SV40 (1100)
 - S BLOOD, SS PHENOTYPE, BREAST CANCER (1130)
 - SARCOMA, FERRIDEXTRAN SPOFA, RAT (0900)
 - SARCOMA, HUMAN ADENOVIRUS TYPE 12, GROWTH ENHANCEMENT, HAMSTER (1050)
 - SERUM, MYELOMA, PROTEINS (LAMBDA) (1127)
 - SPECIFICITY, 3-METHYLCHOLANTHRENE, DIFFERENTIAL ANTIGENICITY SARCOMAS (0942)
 - SURFACE, PROTEIN COMPONENTS, AVIAN TUMOR VIRUS (1085)
 - TUMOR-SPECIFIC, RAT MAMMARY CARCINOMA, ISOLATION (1132)
 - TUMOR-SPECIFIC NEOANTIGEN, VIRUS, HUMAN MAMMARY CARCINOMA (1131)
 - VARIATION, IMMUNOCHEMICAL ANALYSIS, POLYOMA VIRUS (1107)
 - VIRAL, HERPES, CELL MEMBRANES (1062)
 - VIRUS, EPSTEIN-BARR VIRUS, MAREK'S

DISEASE HERPES VIRUS (1028)
 ANTIMETABOLITE
 ALKYLATING AGENTS, ANTIBIOTICS,
 CANCER CHEMOTHERAPY, CARCINO-
 GENICITY, RAT (0906)
 ANUS
 CARCINOMA, PATHOGENESIS, HUMAN
 (1164)*
 AROMATIC HYDROCARBON
 CARCINOGENICITY IN WATER ENVIRONMENT,
 BENZO(A)PYRENE (0865)*
 ASBESTOS
 EXPOSURE, CLINICAL FEATURES,
 DIFFUSE PLEURAL MESOTHELIOMA (1004)
 OCCUPATIONAL EXPOSURE, MESOTHELIOMA,
 SCOTLAND (1170)
 PLEURAL AND PULMONARY ASBESTOSIS,
 EARLY RADIOLOGICAL CHANGES (1263)*
 ASTROCYTOMA
 DNA REPLICATION, HUMAN (1230)
 BACILLUS CALMETTE-GUERIN
 INOCULATION OF BACILLUS, LEUKEMIA
 INCIDENCE (1250)
 MAMMARY TUMOR ENHANCEMENT,
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 (1243)
 VACCINATION, SCOTLAND, LEUKEMIA
 MORTALITY (1251)
 BENZENE
 SINUS LYMPHOCYTES, FOLLICULAR LYMPHO-
 CYTES, HEMOGRAMS (0933)
 BENZIDINE
 CARCINOGENESIS, TRYPTOPHAN METABOLISM,
 3-HYDROXYANTHRANILIC ACID, RAT
 (0911)
 BENZO(A)PYRENE
 3,4-BENZFLUORANTHENE, CARCINOMATOUS
 TISSUE, STOMACH, RECTUM (0912)
 CARCINOGENICITY IN WATER ENVIRONMENT,
 POLYNUCLEAR AROMATIC HYDROCARBONS
 (0865)*
 FIBROSARCOMA TUMOR CELL INOCULA,
 RETARDATION OF PRIMARY TUMOR GROWTH
 (0940)
 LUNG, RATS, METABOLISM, ELIMINATION
 (0936)
 METABOLISM, COLD-BLOODED VERTEBRATES,
 WARM-BLOODED VERTEBRATES (0937)
 METABOLISM, MACROMOLECULE BINDING
 (0941)
 MOUSE TUMOR, IMMUNOBLOBULIN IGG2
 (1133)
 UV RADIATION, DNA, PHOTO ADDUCT (0938)
 WATER SOLUBILITY, EFFECT OF CAFFEINE
 (0989)*
 BENZO(B)THIOPHENE
 DERIVATIVES, CARCINOGENICITY (0863)*
 BERYLLIUM
 CHRONIC INTOXICATION, OCCUPATIONAL
 EXPOSURE, CANCER (0981)
 BETEL-NUT
 BUCCAL MUCOSA, TOBACCO CHEWING (0978)
 CHEWING, TOBACCO CHEWING, HISTOLOGY
 OF BUCCAL MUCOSA (0979)
 BILE DUCT
 CARCINOMA, ULCERATIVE COLITIS (1249)

BLADDER
 CANCER, LOWER URINARY TRACT CANCER,
 CIGARETTE SMOKING (0976)
 TUMORS, 2-ACETYLAMINOFLUORENE,
 DIETARY INDOLE (0907)
 TUMORS, DIETARY BRACKEN FERN, THIAMINE
 (0899)
 TUMORS, TEXTILE WORKERS, HIGH-RISK
 OCCUPATIONS (0980)
 WALL, 3-METHYLBOLANTHRENE, SPECTRO-
 PHOTOMETRY, RAT (0948)
 BONE
 CANCER, RADIUM EXPOSURE, CHILDREN
 (1000)
 PLUTONIUM, RETENTION (1012)
 THORIUM 232, HUMAN (1006)
 239PU EXPOSURE, SPECULATIVE ESTIMATE
 OF HAZARD, TUMOR RISK (1003)
 BONE MARROW
 CHLORAMBUCIL, PROLIFERATION, SERUM,
 RAT (0901)
 7,12-DIMETHYLBENZ(A)ANTHRACENE,
 RADIATION LEUKEMOGENESIS (0928)
 DNASE, MICE, LEUKEMIA, VIRUS (1041)
 HUMAN MYELOMONOCYTIC LEUKEMIA, MICRO-
 CHROMOSOMES (1147)
 IONIZING RADIATION, HUMAN (0993)
 STEM CELL PROLIFERATION, X-IRRADIATION
 (1011)
 BRACKEN FERN
 DIET, DEVELOPMENT OF BLADDER TUMOR,
 THIAMINE (0899)
 BRAIN
 LESIONS, HISTOPATHOLOGY, PROTON-
 IRRADIATION (1007)
 TUMOR ETIOLOGY, HORMONES, REVIEW
 (0844)
 TUMORS, METHYLNITROSOUREA, RAT (0963)
 TUMORS, TRANSPLACENTAL, ETHYLNITRO-
 SOUREA (0964)
 2-BROMO-ALPHA-ERGOCRYPTINE
 ERGOCORINE, MAMMARY HYPERPLASTIC
 NODULE (1207)
 MAMMARY CARCINOMA, ENDOCRINE FUNCTION
 (0930)
 7-BROMOMETHYLBENZ(A)ANTHRACENE
 CARCINOGENICITY (0933)
 7-BROMOMETHYL-12-METHYLBENZ(A)ANTHRACENE
 CARCINOGENICITY (0933)
 BURKITT'S LYMPHOMA
 CHILDREN, TUMORS OF HEAD AND NECK
 (1188)
 EPSTEIN-BARR VIRUS, NASOPHARYNGEAL,
 CARCINOMA (1024)
 NEOCARZINOSTATIN, EPSTEIN-BARR VIRUS,
 VIRUS (1020)
 VIRUS, INCIDENCE, REVIEW (0870)*
 BURSA
 BURSECTOMY, X-IRRADIATION, SPLEEN
 IMMUNE RESPONSE (1134)
 CADMIUM
 CHLORIDE, SUBCUTANEOUS SARCOMA, RAT
 (0898)
 CAFFEINE
 BENZO(A)PYRENE, WATER SOLUBILITY
 (0989)*

CALCIFICATION
BREAST CANCER, FAT TRANSPLANTATION,
HUMAN (1010)

CALCIUM
PROTEIN-BOUND, LYMPHOSARCOMA, EHRLICH
CARCINOMA (1233)

CANAVANINE
ADENOVIRUS, INHIBITION OF REPLICATION
(1046)

CAPSID
PROTEINS, ADENOVIRUS (1043)

CARBON TETRACHLORIDE
HEPATIC LESIONS, 3-METHYLCHOLANTHRENE
(0945)

CARCINOGENESIS
MECHANISM, PROTEIN MODIFICATION
KINETICS, CARCINOGENIC FACTORS
(1162)
MODEL, MALIGNANT TRANSFORMATION
IN VITRO, PHASES OF CELL GROWTH
(0854)

CARCINOGENICITY
7-BROMOMETHYLBENZ(A)ANTHRACENE,
7-BROMOMETHYL-12-METHYLBENZ(A)
ANTHRACENE (0933)
ENHANCED DETECTION, TRANSPLACENTAL
EFFECTS, URETHANE, MOUSE (0972)

CARCINOMA
ANAL FISTULA, PATHOGENESIS (1164)*
CAUSTIC ULCERATION, ESOPHAGUS, BOUGIE
(0988)*
SQUAMOUS CELL, DESMOSOMES, KERATINO-
CYTES, HUMAN (1231)
STOMACH, RECTUM, BENZO(A)PYRENE,
3,4-BENZFLUORANTHENE (0912)

CAROTID BODY
TUMORS, FAMILIAL OCCURRENCE, BILATERAL
TUMOR (1258)

CELL
FUSION, POLYKARYOCYTOSIS, VIRUS (1019)

CENTRAL NERVOUS SYSTEM
INTRACRANIAL MENINGEOMA, FAMILIAL,
HUMAN (1262)

CERVIX
CANCER, ENDOMETRIAL CANCER, ISRAELI
POPULATION (1175)
CANCER, TRICHOMONAS VAGINALIS (1265)*
CERVICO-VAGINAL TUMORS, 7,12-DIMETHYL-
BENZ(A)ANTHRACENE, L-THYROXINE,
METHYLTHIOURACIL, RATS (0887)
DYSPLASIA, CARCINOMA IN SITU, TRANSI-
TION TIME (1157)
EPITHELIUM, MORPHOLOGY, CARCINOGENESIS
HUMAN (0853)
MONKEY, CHRONIC ESTROGENIC STIMULA-
TION, EPIDERMIZATION OF ENDOMETRIUM
(1158)
SQUAMOUS CELL CARCINOMA, SKIN
CARCINOMA, TANZANIA (1176)
VAGINAL TRICHOMONIASIS, PRECANCEROUS
CONDITION (1238)

CHALONE
EPIDERMAL, HAMSTER, SQUAMOUS CELL
CARCINOMA (1216)
EPIDERMAL, SQUAMOUS CELL CARCINOMA,
HAMSTER (1208)

CHEMICAL CARCINOGEN
BINDING TO CELL PROTEIN, TARGET ORGAN
SPECIFICITY, REVIEW (0833)
CR, AS, NI, AROMATIC HYDROCARBONS,
AZO DYES, RADIATION, OCCUPATIONAL
HAZARDS, REVIEW (0878)*
NON-MALIGNANT MORTALITY, TOPICAL
ADMINISTRATION (1191)*
SMOKED FOOD PRODUCTS, REVIEW (0879)*
TUMOR ANTIGENICITY (0843)

CHILDREN
BURKITT'S LYMPHOMA, TUMORS OF HEAD AND
NECK (1188)
RADIUM EXPOSURE, BONE CANCER INDUCTION
(1000)
THYROID CARCINOMA, EPIDEMIOLOGY AND
CLINICAL COURSE (1173)

CHLORAMBUCIL
SERUM, BONE MARROW, PROLIFERATION,
RAT (0901)

5-ALPHA-CHOLEST-6-ENE
5-ALPHA-CHOLESTA-1,3,6-TRIENE,
TUMORIGENESIS IN MICE (0888)
5-ALPHA-CHOLESTA-1,3,6-TRIENE
TUMORIGENESIS IN MICE, 5-ALPHA-
CHOLEST-6-ENE (0888)

CHROMOSOME
ABERRATION, CHROMATID TYPE ABNORMAL-
ITIES, FANCONI'S APLASTIC ANEMIA
(1220)
ABERRATION, LYMPHOCYTE, RADIATION,
HUMAN (1008)
ABERRATION, NEUTRON IRRADIATION,
PIG LEUKOCYTES (1005)
ABERRATION, VIRAL INDUCTION, VIRUS
(0866)*
ABERRATION, X-IRRADIATION, MYXOVIRUS
INFECTION (1002)
ABNORMALITY, FIBROBLASTIC PROLIFERA-
TION, ACUTE MYELOFIBROSIS (1247)
ANOMALY, DNA REPAIR SYNTHESIS,
4-NITROQUINOLINE-1-OXIDE, HUMAN,
HAMSTER (0968)
ANOMALY, NEOPLASTIC TISSUE, COMPUTER
ANALYSIS (1256)
ASCITIC SARCOMA, 3-METHYLCHOLANTHRENE,
HAMSTER (1219)
BREAKAGE, LEUKEMIA, INHERITED DISEASES
(0856)
DAMAGE, BONE MARROW, TRENUM, NUCLEI,
HAMSTERS (0903)
GLIOMA, DOUBLE-MINUTE, HUMAN (1260)
MICRO-, HUMAN MYELOMONOCYTIC LEUKEMIA,
BONE MARROW (1147)
PH1, ACUTE MYELOBLASTIC LEUKEMIA, DI
GUGLIELMO'S SYNDROME (1252)
PH1 CHROMOSOME-NEGATIVE MARROW CELLS,
CHRONIC MYELOCYTIC LEUKEMIA (1235)
RETICULOSARCOMA, CLONAL PROLIFERATION
(1224)
ROUS SARCOMA VIRUS, RAT (1084)
SEX, GONADAL DYSGENESIS, AMENORRHEA,
MALIGNANCY (1261)

COLON
DESMOID TUMORS, POLYPOSIS COLI (1156)
CROTON OIL

- THYMIDINE INCORPORATION,
13-O-TETRADECANOYL-PHORBOL-12-ACE-
TATE (0892)
- CROWN GALL
GENETIC INFORMATION, NUCLEAR DNA,
BACTERIAL DNA, TUMOR TISSUE (1254)
- CYCASIN
LIVER TUMORS, PULMONARY TUMORS (0895)
- CYCLOHEXIMIDE
DNA SYNTHESIS, POLYOMA VIRUS, MOUSE
EMBRYO CELL (1110)
- DIET
FEED, CONTAMINATION, AFLATOXINS B1,
B2, G1, G2 (0991)*
LIPOTROPE-DEFICIENT, LIVER TUMORS,
AFLATOXIN CARCINOGENESIS (0915)
MEXICAN POPULATION IN TEXAS, GALL-
BLADDER CANCER, ETIOLOGY (1171)
RENAL TUMORS, DIMETHYLNITROSAMINE,
RATS (0952)
- DIETHYLNITROSAMINE
HEPATOMAS, STAGES IN MALIGNANT TRANS-
FORMATION (0957)
LIVER, ENZYME HISTOCHEMISTRY, RAT
(0960)
LIVER, HEPATECTOMY, REGENERATION, RAT
(0959)
- DIETHYLSTILBESTROL
CHICKEN LIVER, LYSYL-TRANSFER RNA
(1205)
- DIMETHYLAMINOAZOBENZENE
METABOLITES, DNA BINDING, RAT LIVER
MICROSOMES (0921)
- P-DIMETHYLAMINOAZOBENZENE
LIVER CHANGES, ENZYME ACTIVITY, RAT
(0922)
MICE AND HAMSTERS, AZODYE BINDING TO
LIVER PROTEINS (0923)
- P-DIMETHYLAMINOPHENYLAZODIBENZOTHIOPHENE
CARCINOGENICITY IN RAT LIVER (0924)
- 7,12-DIMETHYLBENZ(A)ANTHRACENE
DIGESTIVE TRACT, MOUSE (0926)
DNA, BENZ(A)ANTHRACENE, BINDING (0934)
LEUKEMOGENESIS, PHORBOL (0893)
MAMMARY TUMORS, PROLACTIN (0927)
MAMMARY TUMOR ENHANCEMENT, BACILLUS
CALMETTE-GUERIN (1243)
MAMMARY TUMOR SUPPRESSION, ACTINOMYCIN
D (0932)
MICE, SKIN, DNA REPLICATION (0931)
RADIATION LEUKEMOGENESIS, BONE MARROW
CELLS (0928)
RESERPINE, MAMMARY TUMOR (0929)
SKIN TUMORS, RIBOFLAVIN DEFICIENCY
(0935)
TESTOSTERONE, OVARECTOMY, MAMMARY
GLAND TUMOR, MOUSE (1145)
L-THYROXINE, METHYLTHIOURACIL,
CERVICO-VAGINAL TUMORS, CASTRATION
(0887)
- DIMETHYLNITROSAMINE
ANIMOACETONITRILE, METABOLISM (0961)
HEPATOMA, ANTIGENICITY, RAT (0956)
KIDNEY, MESENCHYMAL TUMORS, RAT (0950)
RENAL CARCINOMAS, PROTEIN DEFICIENT
RATS (0954)
RENAL TUMORS, DIET, RATS (0952)
- TRANSFORMATION, REVERTANT, LIMITED
LIFE-SPAN, HAMSTER EMBRYO CELL
(0951)
- DNA
ADENOVIRUS TYPE 12, KIDNEY CELLS,
INTEGRATION (1051)
BENZ(A)ANTHRACENE, BINDING (0934)
BENZ(A)PYRENE, PHOTO ADDUCT, UV RADIA-
TION (0938)
BINDING, RAT LIVER MICROSOMES,
DIMETHYLAMINOAZOBENZENE METABOLITES
(0921)
CO-CULTURE, EHRLICH ASCITES, CHINESE
HAMSTER CELLS (1202)
COMPLEX FORMATION, POLYOMA VIRUS,
MOUSE EMBRYO FIBROBLAST (1111)
HYBRID, ADENOVIRUS TYPE 2, SV40 (1052)
POLYMERASE, SARCOMA, MYELOBLASTOSIS,
VIRUS (1081)
POLYOMA VIRUS, THERMOSENSITIVE MUTANT
(1109)
REPAIR SYNTHESIS, CHROMOSOME ANOMALY,
4-NITROQUINOLINE-1-OXIDE, HUMAN,
HAMSTER (0968)
REPLICATION, 7,12-DIMETHYLBENZ(A)
ANTHRACENE, SKIN, MICE (0931)
REPLICATION, RHABDOMYOSARCOMA, ASTRO-
CYTOMA, NEUROBLASTOMA (1230)
RNA IN RAT PROSTATE, PROGESTERONE,
ESTROGEN (0889)
SIMIAN PSEUDO VIRUS, MOUSE EMBRYO CELL
(1094)
- SV40, LENGTH OF VIRAL DNA MOLECULE
(1098)
SV40, MAMMALIAN RNA POLYMERASE (1103)
SV40, VARIANT, TRANSFORMATION, HUMAN
FIBROBLAST CELL (1095)
SYNTHESIS, ADENOVIRUS, HAMSTER KIDNEY
CELL, HUMAN EMBRYO LUNG CELL (1044)
SYNTHESIS, ADENOVIRUS TYPE 12, HAMSTER
(1047)
SYNTHESIS, POLYOMA VIRUS, CYCLO-
HEXIMIDE, MOUSE EMBRYO CELL (1110)
SYNTHESIS, POLYOMA VIRUS, MOUSE
EMBRYO CELL (1106)
SYNTHESIS, SV40, HAMSTER (1089)
SYNTHESIS, SV40 VIRUS, THERMOSENSITIVE
SV40 MUTANT, TEMPERATURE EFFECT
(1090)
SYNTHESIS, UV IRRADIATION DAMAGE,
NON-PROLIFERATING ACUTE LEUKEMIA
CELLS (1223)
TUMOR, GENETIC INFORMATION, BACTERIAL
DNA, NUCLEAR DNA (1254)
WALKER-256 CARCINOSARCOMA, TRANS-
FORMATION REVERSAL (1210)
- EMBRYO
CHICK, NEW AVIAN TUMOR VIRUS, HELPER
FACTOR (1086)
- ENDOMETRIUM
CANCER, CYTOLOGIC STUDY OF ASSOCIATION
HYPOESTROGENISM (1225)
CANCER, ISRAELI POPULATION, CERVICAL
CANCER (1175)
CARCINOMA, FALLOPIAN TUBE, EPITHELIAL
HYPERPLASIA, ESTROGEN (1160)

EPIDERMIZATION, MONKEY CERVIX, CHRONIC
ESTROGENIC STIMULATION (1158)
HYPERPLASIA, HORMONAL CONTRACEPTIVES,
SOMATIC EFFECTS, REVIEW (0871)*

ENVIRONMENTAL FACTOR

CANCER INCIDENCE, CRACOW (1167)
MUTATION, CHEMICAL MUTAGENS (0855)
OCCUPATIONAL HAZARDS, ORGANIC AND
INORGANIC CARCINOGENS, REVIEW
(0877)*

ENZYME

ACID DNASE, LEUKEMIA CELLS, CYTOTOXIC
EFFECT, MICE (1041)
ACID PHOSPHATASE, BETA-GLUCURONIDASE,
AFLATOXIN, LYSOSOMAL ENZYME ACTIVITY
(0916)
ALDOLASE ISOZYME ACTIVITY, NERVOUS
SYSTEM TUMORS (1255)
ARGINASE, ANAEROBIC GLYCOLYSIS,
NEOPLASTIC CONVERSION (1143)
ARYL HYDROCARBON HYDROXYLASE, POLY-
CYCLIC HYDROCARBON, 17-BETA-
ESTRADIOL, MOUSE (0891)
BENZO(A)PYRENE HYDROXYLASE, 3-METHYL-
CHOLANTHRENE, RAT SKIN (0939)
CITRIC ACID CYCLE, LIVER, AFLATOXIN,
MICE (0920)
KREBS CYCLE, DIAPHORASES, PHOSPHATASES
LIVER, DIETHYLNITROSAMINE, RAT (0960)
LACTIC DEHYDROGENASE, EXPERIMENTAL
TUMORS, CLASSIFICATION, MORPHOGENE-
SIS (0966)
LIVER, P-DIMETHYLAMINOAZOBENZENE, ACID
PHOSPHATASE, ESTERASE, SUCCINIC
DEHYDROGENASE (0922)
LYSOSOMAL ACTIVITY, TUMOR GROWTH,
MOUSE MELANOMA (1248)
MICROSOMAL ENZYME, ENVIRONMENTAL
CONTAMINANTS (0848)
NAD TETRAZOLIUM REDUCTASE, LDH,
G6PDH, NERVOUS SYSTEM TUMORS (1196)
NEOPLASM PATHOGENESIS, MODIFICATION
PROCESSES, REVIEW (0860)
PHOSPHATASE, MOUSE MAMMARY TUMORS,
ENZYME DISTRIBUTION (1144)
SIALIC ACID TRANSFERASE, TRANSFORMED
CELLS (1101)
TRNA METHYLASE, ACTIVITY, ADENO-
VIRUS-12, HAMSTER (1049)
TYROSINE HYDROXYLASE ACTIVITY, DOPA,
HAMSTER ISLET CELL TUMORS (1222)

EPIDEMOLOGY

BEDOUINS IN ISRAEL, LIVER CANCER
(1168)
BREAST CANCER RISK, AGE AT FIRST BIRTH
(1187)
CANCER, CRACOW, URBAN AND COUNTRY,
ENVIRONMENT (1167)
CANCER, GERIATRIC PATIENTS, REVIEW
(0869)*
CANCER, MEXICO (1193)*, (1194)*,
(1195)*
CANCER, NORWAY (1190)*
CANCER, REVIEW (0873)*
CARCINOMA OF THE COLON, EASTERN AND
WESTERN NATIONS, INTESTINAL BACTERIA
(1189)

CHILDHOOD CANCER, WILM'S TUMOR,
CLINICAL FEATURES (1180)
CHILDREN, THYROID CARCINOMA (1173)
CHINESE-BORN POPULATION OF SINGAPORE,
LIVER CANCER (1165)
GEOGRAPHIC DIFFERENCES, HISTOLOGICAL
ORIGIN OF CANCER (0858)
IMMIGRANT POPULATIONS, CANCER SITES
(0857)

IRAN, DISTRIBUTION OF CANCER, AFFECTED
SITE (1179)

ISRAELI POPULATION, ENDOMETRIAL AND
CERVICAL CANCER (1175)

LEUKEMIA, KENYA (1166)

MEXICAN POPULATION IN TEXAS, GALL-
BLADDER CANCER, DIET (1171)

MISSOURI, ANNUAL CANCER FREQUENCIES
(1181)

MORTALITY RATES, CANCER OF THE
PANCREAS, CIGARETTE SMOKING (1178)

MORTALITY RATES, CHILE, ESOPHAGEAL AND
GASTRIC CANCER (1169)

MORTALITY RATES, TESTICULAR TUMOR,
MAN, TREATMENT (1186)

NEOPLASTIC DISEASES, REVIEW (0868)*
NON-WHITE AMERICANS, AMERICAN MORTAL-
ITY DISTRIBUTION, ESOPHAGEAL CANCER
(1181)

OCCUPATIONAL EXPOSURE, NICKEL,
COBALT, LUNG CANCER (1185)

POLAND, PULMONARY CANCER (1192)*
PRIMARY LUNG CANCER, ALESSANDRIA
(1184)

SMOKING, CARCINOMA OF THE TONGUE
(0847)

SOY BEAN PASTE, KOREA, STOMACH CANCER
(1174)

EPIDIDYMS

ADENOMATOID TUMOR, MESOTHELIAL ORIGIN,
ULTRASTRUCTURE (1161)

EPITHELIOMA

MAMMARY GLAND, CHRONIC CYSTIC MASTITIS
MALIGNANT TRANSFORMATION (1159)

EPITHELIUM

CERVIX UTERI, MORPHOLOGY, CARCINOGENE-
SIS, HUMAN (0853)

TRACHEA, MORPHOLOGY, VITAMIN A
DEFICIENCY, METAPLASIA, RAT (1209)

ERGOCORNINE

2-BROMO-ALPHA-ERGOCRYPTINE, MAMMARY
HYPERPLASTIC NODULE (1207)

ERYTHROCYTE

OSMOTIC FRAGILITY, FRIEND LEUKEMIA
VIRUS (1033)

ESOPHAGUS

CANCER, GASTRIC SURGERY, RECTAL CANCER
(1228)

CANCER, NON-WHITE AMERICANS, AMERICAN
MORTALITY DISTRIBUTION (1181)

CARCINOMA, CAUSTIC ULCERATION, MAN
(0988)*

EPITHELIOMA, CAUSTIC STENOSIS, MAN
(1154)

PRECANCEROUS STATES, CICATRITION,

- PEPTIC STENOSIS, SURGERY (0851)
 ESTRADIOL
 ADRENOCORTICAL CARCINOMA, RAT (0890)
 17-BETA-ESTRADIOL
 ARYL HYDROCARBON HYDROXYLASE, POLY-
 CYCLIC HYDROCARBONS, MOUSE (0891)
 ESTROGEN
 CHANGES IN RAT UTERUS, INTRAUTERINE
 CONTRACEPTIVE DEVICE (0985)
 TUMOR, HORMONE RESPONSIVENESS, BINDING
 (0834)
 ETHYL METHANESULFONATE
 METABOLISM, MOUSE (0902)
 ETHYL-NITROSOUREA
 TRANSPLACENTAL, BRAIN TUMORS (0964)
 ETIOLOGY
 BRONCHIAL CARCINOMA, REVIEW (0872)*
 CANCER, REVIEW (0883)*
 EYE
 CONJUNCTIVAL LESIONS, AFRICAN PATIENT,
 PINGUECULA (1213)
 FALLOPIAN TUBE
 EPITHELIAL HYPERPLASIA, ENDOMETRIAL
 CARCINOMA, ESTROGEN (1160)
 FAMILIAL POLYPOSIS
 COLON, CARCINOMA OF THE RECTUM,
 HEREDITARY DISTRIBUTION (1245)
 COLON, DESMOID TUMORS (1156)
 FANCONI'S ANEMIA
 CHROMOSOME ABERRATIONS, CHROMATID TYPE
 ABNORMALITIES (1220)
 FERRIDEXTRAN SPOFA
 SARCOMA, ANTIGENICITY, RAT (0900)
 FIBROBLAST
 SV40, POLYOMA VIRUS, GLYCOLIPIDS
 (1102)
 FIBROSARCOMA
 ALPHA PARTICLE IRRADIATION, RAT (0992)
 GALLBLADDER
 CANCER, MEXICAN POPULATION IN TEXAS,
 DIETARY ETIOLOGY (1171)
 GANGLIONEUROMA
 RAT ADRENAL MEDULLA, PREOPTIC-ANTERIOR
 HYPOTHALAMIC LESION (1259)
 GANGLIOSIDE
 ALTERATION, SV40, POLYOMA VIRUS (1091)
 GASTROINTESTINAL TRACT
 DMBA, PENETRATION-FIXATION, MESENTERIC
 TUMORS (0926)
 ESOPHAGEAL AND GASTRIC CANCER, CHILE,
 MORTALITY RATES (1169)
 LUNG, BENZO(A)PYRENE, 3,4-BENZFLUOR-
 ANTHENE, CARCINOMA TISSUE (0912)
 GENETICS
 CARCINOMA OF THE RECTUM, FAMILIAL
 POLYPOSIS OF THE COLON (1245)
 DIZYGOTIC TWINS, MONOZYGOTIC TWINS,
 TUMOR DEVELOPMENT (0861)
 FAMILIAL OCCURRENCE, CAROTID BODY
 TUMORS, BILATERAL TUMOR (1258)
 HYBRIDIZATION, KARYOLOGIC CHARACTER-
 ISTICS, MICE (0838)
 HYBRIDIZATION, NUCLEAR DNA, BACTERIAL
 DNA, TUMOR TISSUE (1254)
 LETHAL YELLOW GENE, RAT RETICULAR
 TUMOR DEVELOPMENT (1198)
 MENINGEOMA, FAMILIAL, INTRACRANIAL
 (1262)
 VIRAL, LETHAL MUTATION (0864)*
 GLIOMA
 CHROMOSOME, DOUBLE-MINUTES, HUMAN
 (1260)
 TYPE C VIRUS, HUMAN (1018)
 GLOMUS
 TUMOR, ULTRASTRUCTURE, HISTOGENESIS
 (1227)
 GROWTH
 ENZYME ACTIVITY, MOUSE MELANOMA,
 LYSOSOMAL ENZYME ACTIVITY (1248)
 FACTOR, CHALONE, SQUAMOUS CELL
 CARCINOMA (1208), (1216)
 INHIBITION, WALKER 256 CARCINOSARCOMA
 ZINC-DEFICIENT DIET (1232)
 PHASES, MALIGNANT TRANSFORMATION
 IN VITRO, METABOLIC CHANGES (0854)
 POLYOMA VIRUS, PROTEIN SYNTHESIS,
 DENSITY (1108)
 RETICULUM CELL SARCOMA, LYMPHOSARCOMA
 LYMPH NODE (1236)
 HAIR
 FOLLICLE, HISTOGENESIS, BASAL CELL
 EPITHELIOMA (0862)*
 HAND
 SKIN OF ARM AND HAND, SQUAMOUS CELL
 CARCINOMA OF SKIN, SUNLIGHT (0997)
 HEAD
 NECK, SQUAMOUS CELL, CARCINOMA,
 TOBACCO (0850)
 NECK TUMORS, CHILDREN, BURKITT'S
 LYMPHOMA (1188)
 HEART
 CARDIAC MYXOMA, ULTRASTRUCTURE OF
 LESION (1253)
 HEPATOMA
 DIETHYLNITROSAMINE, ANTIGENICITY, RAT
 (0956)
 HERBICIDE
 MONURON, CARCINOGENICITY, RAT, MOUSE
 (0897)
 HISTOGENESIS
 CANCER, EPIDEMIOLOGY, GEOGRAPHIC
 DIFFERENCES (0858)
 HAIR FOLLICLE, BASAL CELL EPITHELIOMA
 (0862)*
 HODGKIN'S DISEASE
 AGE DISTRIBUTION (1218)
 ANTIBODY TITERS, EPSTEIN-BARR VIRUS
 (1025)
 HISTOLOGICAL EVOLUTION (1148)
 HORMONE
 ANDROGEN TREATMENT, PRAOMYS (MASTOMYS)
 NATALENSIS, PROSTATIC HYPERPLASIA
 (0885)
 2-DR-ALPHA-CRYPTINE, GROWTH, MAMMARY
 CARCINOMA (0930)
 CHRONIC ESTROGENIC STIMULATION,
 EPIDERMIZATION OF ENDOMETRIUM,
 MONKEY CERVIX (1158)
 CONTRACEPTIVES, ENDOMETRIUM, REVIEW
 (0871)*
 ESTROGEN, BINDING, TUMOR RESPONSIVE-
 NESS (0834)
 ESTROGEN, ENDOMETRIAL CARCINOMA,

FALLOPIAN TUBES, EPITHELIAL HYPERPLASIA (1160)
 HYPOESTROGENISM, ENDOMETRIAL CANCER, CYTOLOGIC STUDY (1225)
 HYPOTHYROIDISM, HYPERESTRINISM, 6-METHYLTHIOURACIL, MAMMARY GLAND CANCER, RAT (0886)
 METHYLTHIOURACIL, L-THYROXINE, CASTRATION, DMBA, CERVICO-VAGINAL TUMORS IN RATS (0867)
 OVARY, PULMONARY TUMORS, HYDRAZINE SULFATE (0910)
 POSTCASTRATIONAL ADRENAL TUMORS, STRAIN VARIABILITY, MICE (1199)
 PREGNANCY, 5-HYDROXYTRYPTAMINE, MAMMARY TUMOR DEVELOPMENT (1226)
 PROGESTERONE, ESTROGEN, DNA AND RNA IN RAT PROSTATE (0889)
 STEROID EQUILIBRIUM, BRAIN TUMORS, ETIOLOGY, REVIEW (0844)
 STIMULATION OF TUMORIGENESIS, MAMMARY TUMOR (1215)
 TESTOSTERONE, SYNESTROL, 7,12-DIMETHYLBENZ(A)ANTHRACENE, MAMMARY GLAND TUMOR, MOUSE (1145)
 TUMOR GROWTH, OVARIECTOMIZED RATS, YOSHIDA ASCITES SARCOMA (1214)
 HYBRIDIZATION
 MICE, CARCINOGENESIS, KARYOLOGIC CHARACTERISTICS, HEREDITY (0838)
 HYDRAZINE
 SULFATE, OVARIAN HORMONE PRODUCTION, PULMONARY TUMORS (0910)
 HYDROCARBON
 CARCINOGENIC, NITROSAMINES, SPINACH (0880)*
 N-HYDROXY-2-ACETAMIDOFLOURENE
 EXCRETION, ADRENALECTOMY, BILE DUCT LIGATION (0908)
 3-HYDROXYANTHRANILIC ACID
 EARLY BENZIDINE CARCINOGENESIS, SERUM, RAT (0911)
 5-HYDROXYTRYPTAMINE
 MAMMARY TUMOR DEVELOPMENT (1226)
 HYPERPLASIA
 LIPID, RAT ADRENAL CORTEX, ANILINE (0925)
 IATROGENIC TUMOR
 CYTOSTATICS, IMMUNOSUPPRESSIVES, RATS (0904)
 IMMUNITY
 HUMAN CANCER, TUMOR SPECIFIC ANTIGENS (0840)
 IMMUNOLOGICAL ABNORMALITIES, SIBLING GROUP, LYMPHORETICULAR MALIGNANCIES (1123)
 LYMPHOCYTES, PHYTOHEMAGGLUTININ (1137)
 TRANSPLANTATION, TUMOR CELL EXTRACTS, ADENOVIRUS 12 (1055)
 IMMUNOGLOBULIN
 IGG2, BENZO(A)PYRENE-INDUCED MOUSE TUMORS (1133)
 IGM DYSPROTEINEMIA, ACUTE MYELOMA (1128)
 URINE, CANCER PATIENTS, LIGHT CHAIN (1139)

IMMUNOLOGY

ADENOVIRUS TYPE 8, TYPE 9, CROSS REACTIVITY (1054)
 ANTIBODY TO FLAGELLIN, CANCER PATIENTS, SURVIVAL TIME (1119)
 ANTIGENICITY, SPONTANEOUSLY TRANSFORMING MOUSE CELLS (1120)
 ANTITUMOR ANTIBODIES, SARCOMAS IN MICE METHYLCHOLANTHRENE (0943)
 CANCER, RESISTANCE TO TUMOR (1142)*
 CARCINOMA, OVARY, UTERUS, MAMMARY GLAND (1135)
 CROSS-REACTION, AVIAN LEUKOSIS GROUP-SPECIFIC ANTIGEN, HUMAN LEUKEMIC PLASMA (1126)
 HOST RESPONSE TO TUMOR TRANSPLANT, REGIONAL LYMPH NODES (1125)
 IMMUNE RESPONSE, MINERAL OIL TUMORIGENESIS, SUSCEPTIBILITY (0894)
 MOUSE EMBRYO FIBROBLAST CULTURE, VIRAL ETIOLOGY FOR "SPONTANEOUS" TRANSFORMATION (1072)
 POLYOMA VIRUS, TRANSFORMED MOUSE CELLS, IMMUNE SERUM TREATMENT (1104)
 RETICULOENDOTHELIAL SYSTEM, VIRUS (0882)*
 THYMUS, LYMPHOCYTES, IRRADIATION, MICE (0842)
 TUMOR CELL INOCULA, RETARDATION OF PRIMARY TUMOR GROWTH, BENZO(A)PYRENE (0940)
 TUMOR IMMUNE RESPONSE IN HUMANS, TUMOR ANTIGENICITY (0841)
 IMMUNOSUPPRESSION
 ALKYLATING AGENTS, RATS, MICE (0906)
 CARCINOMA PATIENTS, SUPPRESSION OF IMMUNOCOMPETENCE, SURGERY (1116)
 CYTOSTATICS, CARCINOGENIC EFFECTS, RATS (0904)
 ORGAN TRANSPLANTATION, MALIGNANT TUMORS (0839)
 PAPOVA SV40 VIRUS, HUMAN ADENOVIRUS TYPE 16, SENDAI VIRUS, HAMSTER (1042)
 POLYOMA VIRUS, RESTORATION OF IMMUNOCOMPETENCE (1117)
 THERAPY, ORGAN TRANSPLANT, DEVELOPMENT OF MALIGNANCY (1118)
 TUMOR, POLYOMA VIRUS (1113)
 INOLE
 DIETARY, 2-ACETYLAMINOFLOURENE, URINARY BLADDER TUMORS (0907)
 INFECTIOUS MONONUCLEOSIS
 ACUTE LYMPHATIC LEUKEMIA, CONCURRENT COURSES OF DISEASE (1237)
 INFECTIVITY
 MURINE SARCOMA, VIRUS, TRANSFORMATION (1068)
 INTERFERON
 CHICKEN LEUKOCYTES, HUMAN ADENOVIRUS TYPE 12 (1045)
 EMBRYO CELLS, POLYINOSINIC POLYCYTIDYLIC ACID, VIRUS (0953)
 INTESTINE
 BACTERIA, CARCINOMA OF THE COLON, EASTERN AND WESTERN NATIONS (1189)

- RECTAL CANCER, GASTRIC SURGERY,
ESOPHAGEAL CANCER (1228)
ULCERATIVE COLITIS, BILE DUCT
CARCINOMA (1249)
- KIDNEY
CELLS, RNA SYNTHESIS INHIBITION,
H-1 VIRUS, HUMAN (1099)
GLOMERULONEPHRITIS, GROSS LEUKEMIA
VIRUS, ANTIBODIES, MOUSE (1034)
MESENCHYMAL TUMORS, RAT, DIMETHYL-
NITROSAMINE (0950)
RENAL ADENOCARCINOMA, TUMOR-FREE
POPULATION, LEOPARD FROG (0896)
RENAL CARCINOMAS, PROTEIN DEFICIENT
RATS, DIMETHYLNITROSAMINE (0954)
TUMORS, DIET, DIMETHYLNITROSAMINE,
RATS (0952)
- LACRIMAL GLAND
TUMOR, MALIGNANT TRANSFORMATION (1149)
- LARYNX
LARYNGITIS, CHRONIC, PAPILLOMA, PRE-
CANCEROUS CHANGES (1152)
- LEUKEMIA
ACUTE, MELANOMA, ANTIGENICITY (1129)
ACUTE, NON-PROLIFERATING CELLS, DNA,
UV IRRADIATION (1223)
ACUTE, PROLIFERATIVE KINETICS,
METHODS, REVIEW (0876)*
ACUTE LYMPHATIC, INFECTIOUS MONO-
NUCLEOSIS, CONCURRENT COURSES OF
DISEASE (1237)
ACUTE MONOMYELOGENOUS, AVIAN LEUKOSIS
GROUP-SPECIFIC ANTIGEN, IMMUNOLOGIC
CROSS-REACTION (1126)
ACUTE MYELOBLASTIC, DI GUGLIELMO'S
SYNDROME, PH1 CHROMOSOME CONDITION
(1252)
ANTIGEN, ISOLATION, MAN (1141)*
ANTIGEN, THYMUS-LYMPHOID TISSUE (1121)
AVIAN MYELOBLASTOSIS VIRUS, TRANS-
FORMED CELLS, RNA (1026)
CHRONIC LYMPHOCYTIC, LYMPHOID CELL,
ELECTROPHORETIC PATTERNS (1212)
CHRONIC MYELOCYTIC, PH1 CHROMOSOME-
NEGATIVE MARROW CELLS (1235)
FRIEND VIRUS, SPLEEN (1022)
GRAFFI VIRUS, MYELOGENOUS, MICE (1040)
GUINEA PIG, VIRUS (1039)
HUMAN, MYELOMONOCYTIC, BONE MARROW,
MICROCHROMOSOMES (1147)
INCIDENCE, BACILLUS CALMETTE-GUERIN,
INOCULATION OF BACILLUS (1250)
INCIDENCE IN KENYA (1166)
INHERITED DISEASES, CHROMOSOMAL
BREAKAGE (0856)
LEUKEMOGENESIS, 7,12-DIMETHYLBENZ(A)
ANTHRACENE, PHORBOL (0893)
LYMPHOBLAST, TRNA (1204)
LYMPHOBLASTIC, ACID DNASE, CYTOTOXIC
EFFECT, MICE (1041)
LYMPHOMA, IMMUNOLOGICAL ABNORMALITIES,
SIBLING GROUP (1123)
MORTALITY, BACILLUS CALMETTE-GUERIN
VACCINATION, SCOTLAND (1251)
MYELOPROLIFERATIVE DISEASE, ABNORMAL
CYTOLOGY (1146)
- RETICULOENDOTHELIOSIS, DISTRIBUTION
OF CELLS IN TISSUES, NEOPLASTIC CELL
(1240)
SQUAMOUS CELL CARCINOMA, 3-METHYL-
CHOLANTHRENE, MICE (0949)
TRANSFORMATION, NORMAL MARROW CELL
GRAFT (1201)
VIRAL ETIOLOGY, MAN, REVIEW (0867)*
VIRUS, MAGNESIUM ACETATE, MANGANESE
ACETATE (1037)
VIRUS, MURINE SARCOMA, RNA (1076)
X-RAY RADIATION, HYDROCORTISONE, MICE
(0999)
- LEUKOCYTE
ARTIFICIAL LYMPHOID CELLS, PRELYMPHOMA-
TOUS CONDITION, SFZARY SYNDROME
(1206)
CHROMOSOME ABERRATIONS, NEUTRON
IRRADIATION, PIG (1005)
CLOSED HUMAN, EPSTEIN-BARR VIRUS
ANTIGEN (1021)
- LEUKOPLAKIA
LYMPHOCYTES, ORAL MUCOSA (1150)
- LIPID
GLYCOLIPIDS, SV40, POLYOMA VIRUS,
FIBROBLASTS (1102)
- LIVER
CANCER, BEDOUINS IN ISRAEL, PATHOLOGY
AND EPIDEMIOLOGY (1166)
CANCER, CHINESE-BORN POPULATION OF
SINGAPORE (1165)
CELL CULTURE, AFLATOXIN B1, INHIBITION
OF RNA SYNTHESIS (0914)
CIRRHOSIS, CORTISONE THERAPY, CANCER
(1163)*
DIETHYLNITROSAMINE, HEPATECTOMY, RAT
(0959)
DIETHYLNITROSAMINE CARCINOGENESIS,
ENZYMES, RAT (0960)
DIETHYLSTILBESTEROL, LYSYL-TRANSFER
RNA, CHICKEN (1205)
P-DIMETHYLPHENYLAZODIBENZOTHIOPHENE,
CARCINOGENICITY, RAT (0924)
P-DIMETHYLAMINOAZOBENZENE, ENZYME
ACTIVITY IN RAT (0922)
ENVIRONMENTAL CONTAMINANTS, MICROSOMAL
ENZYMES (0848)
ENZYME ACTIVITY, CITRIC ACID CYCLE,
AFLATOXIN (0920)
HEPATIC CANCER, MYCOTOXIN NUCLEIC ACID
SYNTHESIS, FOOD (0849)
HEPATOCARCINOMA, MONKEY, ULTRASTRUCTURE,
N-NITROSODIETHYLAMINE (0955)
HEPATOMA, REGENERATION, URETHAN, MOUSE
(0971)
HEPATOMA, STAGES IN MALIGNANT TRANS-
FORMATION, DIETHYLNITROSAMINE (0957)
LESIONS, CARBON TETRACHLORIDE,
3-METHYLCHOLANTHRENE (0945)
LIPOTROPE-DEFICIENT DIET, AFLATOXIN
CARCINOGENESIS (0915)
LUNG, MONURON CARCINOGENICITY, RAT,
MOUSE (0897)
METABOLISM, DEGRADATION PRODUCTS,
AFLATOXINS (0917)
MICROSOMAL MEMBRANE, NUCLEIC ACID,
CHEMICAL CARCINOGEN, RAT (0913)

N-NITROSODIMETHYLAMINE, TUMORIGENESIS,
MASTOMYS (0958)
PROTEIN, P-DIMETHYLAMINOAZOBENZENE,
BINDING, MICE AND HAMSTERS (0923)
THIOACETAMIDE, TUMORS, MICE (0969)
TUMORS, CYCASIN, PULMONARY TUMORS
(0895)
TUMORS, METABOLIC CHANGES, THIOACETA-
MIDE (0970)
239PU EXPOSURE, SPECULATIVE ESTIMATE
OF HAZARD, TUMOR RISK (1003)

UNG

BENZO(A)PYRENE, RATS, METABOLISM
(0936)
BRONCHIOLO-ALVEOLAR TUMORS, FILTERED
CIGARETTES, DOGS (0973), (0974)
BRONCHUS, CARCINOMA, ETIOLOGY, REVIEW
(0872)*
CANCER, NICKEL, COBALT, OCCUPATIONAL
EXPOSURE (1185)
CANCER, PREVALENCE RATES, BULLOUS
DISEASE (1221)
CHANGES, RADIATION DAMAGE (1009)
EARLY RADIOLOGICAL CHANGES, PULMONARY
AND PLEURAL ASBESTOSIS (1263)*
GLASS FIBERS, OCCUPATIONAL HAZARD,
CANCER REVIEW (0874)*
MESOTHELIOMA, SILICOSIS, RADIATION
(0996)
NEOPLASIA, OZONE, MICE (0884)
PRIMARY CANCER, EPIDEMIOLOGY,
ALESSANDRIA (1184)
PULMONARY CANCER, POLAND, INCIDENCE
AND MORTALITY (1192)*
PULMONARY TUMORS, HYDRAZINE SULFATE,
OVARIAN HORMONE PRODUCTION (0910)
RESPIRATORY FUNCTION, SPUTUM CYTOLOGY
EXAMINATION, WOMEN CIGARETTE SMOKERS
(0975)
RETENTION IN ORGANS, BEAGLE DOGS,
STRONTIUM 90 (1013)
SCLEROTIC FOCI, PNEUMOCONIOSIS,

NEOPLASTIC TRANSFORMATION (1153)
TUMORS, LIVER TUMORS, CYCASIN (0895)

YMPH NODE

CELLS, SV40, ANTIBODY (1097)
LYMPHOSARCOMA, RETICULUM CELL SARCOMA
(1236)

REGIONAL, HOST RESPONSE TO TUMOR
TRANSPLANT (1125)

YMPHOBLAST

EPSTEIN-BARR VIRUS, INFECTIVITY AND
CYTOPATHOLOGY (1023)
LEUKEMIA, TRNA (1204)

YMPHOCYTE

AGGREGATE ENZYME, RNA SYNTHESIS,
PHYTOHEMAGGLUTININ, HUMAN (1138)
BENZENE, IRON METABOLISM, SINUS,
FOLLICULAR (0983)
CHROMOSOME, ABERRATION, RADIATION,
HUMAN (1008)
LYMPHOMA, MORPHOLOGICAL AND FUNCTIONAL
CHANGES (1257)
NORMAL AND NEOPLASTIC LYMPHOID CELL
PROTEINS, ELECTROPHORETIC PATTERNS
(1212)

ORAL MUCOSA, LEUKOPLAKIA (1150)
PHYTOHEMAGGLUTININ, IMMUNITY (1137)
PHYTOHEMAGGLUTININ, SPLEEN, THYMUS
(1122)
SENSITIZATION, BASIC PROTEIN ANTIGENS,
CANCER TEST (1197)
THYMUS, MICE, IMMUNOLOGY (0842)

LYMPHOMA

EPSTEIN-BARR VIRUS, INFECTIOUS MONO-
NUCLEOSIS, HUMANS (0875)*
GROSS VIRUS, ANTITHYMOCYTE SERUM
(1035)
HUMAN, HOUSEHOLD QUESTIONNAIRE SURVEY,
DOMESTIC CATS (1182)
MORPHOLOGICAL AND FUNCTIONAL CHANGES,
LYMPHOCYTES IN CULTURE (1257)
MURINE, MOLONEY LEUKEMIA VIRUS (1077)
MYELOMA HYBRID, ANTIGEN, PROTEIN
SYNTHESIS (1124)

LYMPHOSARCOMA

EHRLICH'S CARCINOMA, PROTEIN-BOUND
CALCIUM (1233)
LYMPH NODE, RETICULUM CELL SARCOMA
(1236)
NEWBORN AND WEANED MICE, N-NITRO-
SOMETHYLUREA (0962)

MACROPHAGE

ALVEOLAR, BENZO(A)PYRENE, RATS, LUNG
(0936)

MAMMARY GLAND

BILATERAL CANCER, INCIDENCE, PATH-

OLOGY (1266)*
BREAST CANCER, CALCIUM DEPOSITS,
X-RAY, FAT TRANSPLANTATION (1010)
BREAST CANCER RISK, AGE AT FIRST
BIRTH, GLOBAL EPIDEMIOLOGICAL STUDY
(1187)
CANCER, 6-METHYLTHIOURACIL, HYPO-
THYROIDISM, HYPERESTRINISM, RAT
(0886)
CANCER, SS PHENOTYPE, S BLOOD-ANTIGENS
(1130)
CARCINOMA, HUMAN, VIRUS, TUMOR-
SPECIFIC NEOANTIGEN (1131)
CARCINOMA, ORAL CONTRACEPTIVES (0984)
CARCINOMA, TUMOR-SPECIFIC ANTIGEN, RAT
(1132)
CARCINOMA GROWTH, 2-BR-ALPHA-ERGO-
CRYPTINE, ENDOCRINE FUNCTION (0930)
7,12-DIMETHYLBENZ(A)ANTHRACENE, TESTO-
STERONE, OVARECTOMY, MOUSE (1145)
EPITHELIOMA, CHRONIC CYSTIC MASTITIS,
MALIGNANT TRANSFORMATION (1159)
HYPERPLASTIC NODULE, ERGOCORINE,
2-BROMO-ALPHA-ERGOCRYPTINE (1207)
MILK, MAMMARY TUMOR VIRUS (1067)
SPINDLE CELL BREAST SARCOMA,
RHABDOMYOSARCOMATOUS INCLUSIONS,
METAPLASTIC INCLUSIONS (1264)*
TUMOR, HORMONES, STIMULATION OF
TUMORIGENESIS (1215)
TUMOR, PHOSPHATASE ENZYMES, ENZYME
DISTRIBUTION, MOUSE (1144)
TUMOR, PREGNANCY, 5-HYDROXYTRYPTAMINE
(1226)
TUMOR, PROLACTIN, 7,12-DIMETHYLBENZ-

(A)ANTHRACENE (0927)
 TUMOR, RESEPPINE, 7,12-DIMETHYLBENZ-
 (A)ANTHRACENE (0929)
 TUMOR ENHANCEMENT, 7,12-DIMETHYLBENZ-
 (A)ANTHRACENE, BACILLUS CALMETTE-
 GUERIN (1243)
 TUMOR SUPPRESSION, 7,12-DIMETHYLBENZ-
 (A)ANTHRACENE, ACTINOMYCIN D (0932)
 MAREK'S DISEASE
 CYTOPATHIC EFFECT, HERPES TYPE VIRUS,
 VIRUS (1030)
 HERPES-TYPE VIRUS (1031)
 HERPES-TYPE VIRUS, VIRUS PROPAGATION
 IN CULTURE (1029)
 MELANOMA
 ACUTE LEUKEMIA, ANTIGENICITY IN HUMAN
 TUMORS (1129)
 EXPOSURE TO SUNLIGHT (0835)
 LYSOSOMAL ENZYME ACTIVITY, TUMOR
 GROWTH, MOUSE (1248)
 MELANOCYTOMA, NEVOCYTOMA, REVIEW
 (0646)
 MEMBRANE
 MICROSOME, LIVER, NUCLEIC ACID,
 CHEMICAL CARCINOGEN, RAT (0913)
 TUMOR CELL, SIALIC ACID TRANSFERASE
 (1101)
 MENINGEOMA
 INTRACRANIAL, FAMILIAL, SURGERY (1262)
 MESENCHYMAL TUMORS
 DIMETHYLNITROSAMINE, KIDNEY, RAT
 (0950)
 MESOTHELIOMA
 DIFFUSE PLEURAL, ASBESTOS EXPOSURE,
 CLINICAL FEATURES (1004)
 SCOTLAND, OCCUPATIONAL EXPOSURE TO
 ASBESTOS (1170)
 METABOLISM
 CHANGES, THIOACETAMIDE, LIVER TUMORS
 (0970)
 DIMETHYLNITROSAMINE, AMINOACETONITRILE
 (0961)
 ELIMINATION, 4-NITROQUINOLINE-1-OXIDE,
 RAT (0967)
 GLYCOLYSIS, RAT EMBRYO FIBROBLASTS,
 ADENOVIRUS TYPE 12, 6, 3, HAMSTER
 SARCOMA (1048)
 METHYL METHANESULFONATE, ETHYL
 METHANESULFONATE, MOUSE (0902)
 METAL
 MAGNESIUM CHLORIDE, ENHANCED PLAQUE
 FORMATION, VIRUS, ADENOVIRUS (1053)
 METAPLASIA
 TRACHEAL EPITHELIUM, MORPHOLOGY,
 VITAMIN A DEFICIENCY, RAT (1209)
 METASTASIS
 ROUS SARCOMA, VIRUS, CHROMOSOME, RAT
 (1084)
 METHYL METHANESULFONATE
 METABOLISM, MOUSE (0902)
 METHYLATION
 TRANSFER RNA METHYLASES, CANCER,
 REVIEW (0831)
 TRNA, NEOPLASIA, MICE (1200)
 3-METHYLCHOLANTHRENE
 ANTIGENIC SPECIFICITY, DIFFERENTIAL

ANTIGENICITY SARCOMAS (0942)
 ASCITIC SARCOMA, CYTOGENETICS, HAMSTER
 (1219)
 CARBON TETRACHLORIDE, HEPATIC LESIONS
 (0945)
 7,12-DIMETHYLBENZANTHRACENE, ARYL
 HYDROCARBON HYDROXYLASE, MOUSE,
 ESTRADIOL (0891)
 GUH ARABIC, BOVINE SERUM, GUINEA PIG
 (0946)
 RAT SKIN, BENZO(A)PYRENE HYDROXYLASE
 (0939)
 SARCOMAS IN MICE, ANTITUMOR ANTIBODIES
 (0943)
 SPECTROPHOTOMETRY, BLADDER WALL, RAT
 (0948)
 SQUAMOUS CELL CARCINOMA, LEUKEMIA IN
 MICE (0949)
 STOMACH CANCER, INDUCTION, SPECIFIC
 LOCATION (0947)
 THYROIDITIS INDUCTION (0944)
 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE
 TRANSPLACENTAL EFFECTS, PARTIAL
 HEPATECTOMY, RAT (0987)*
 METHYLNITROSOUREA
 BRAIN TUMORS, MORPHOLOGY, RAT (0963)
 N-METHYL-N-NITROSOUREA
 NERVE TUMORS, RATS (0965)
 1-METHYL-1-NITROSOUREA
 PHENYL-DIMETHYL-TRIAcene, NEURINOMA,
 LACTATE DEHYDROGENASE, RAT (0966)
 6-METHYLTHIOURACIL
 MAMMARY GLAND CANCER, HYPOTHYROIDISM,
 HYPERESTRINISM, RAT (0886)
 MICROsome
 LIVER, DIMETHYLAMINOAZOBENZENE META-
 BOLITES, DNA BINDING (0921)
 MINERAL OIL
 OCCUPATIONAL EXPOSURE, CARCINOMA OF
 THE SCROTUM (0859)
 TUMORIGENESIS, SUSCEPTIBILITY, IMMUNE
 RESPONSE (0894)
 MITOCHONDRIA
 ANNULATE LAMELLAE, PARATHYROID ADENOMA
 (1246)
 MITOSIS
 BLOCK, PHYTOHEMAGGLUTININ STIMULATION,
 CELL DEATH, RADIATION (1136)
 INDEX, NEUROBLASTOMA CELLS, CELL
 PROLIFERATION (1242)
 MORPHOLOGY
 EPITHELIUM, CERVIX UTERI, CARCINO-
 GENESIS, HUMAN (0853)
 TRANSITIONS, LYMPHOMA, LYMPHOCYTES IN
 CULTURE (1257)
 MOUTH
 ORAL MUCOSA, LYMPHOCYTES, LEUKOPLAKIA
 (1150)
 MUTATION
 ENVIRONMENTAL HAZARD, CHEMICAL MUTAGEN
 (0855)
 LETHAL, VIRAL GENETIC MATERIAL (0864)*
 MYCOTOXIN
 HEPATIC CANCER, AFLATOXIN, NUCLEIC

ACID SYNTHESIS (0849)
 MYELOBLASTOSIS
 SARCOMA, DNA POLYMERASE, VIRUS (1081)
 MYELOFIBROSIS
 ACUTE, CHROMOSOME ABNORMALITY, FIBRO-
 BLASTIC PROLIFERATION (1247)
 MYELOMA
 IGM, DYSPROTEINEMIA, IGG, SERUM (1128)
 SERUM, PROTEINS (LAMBDA) (1127)
 MYELOPROLIFERATIVE DISEASE
 ABNORMAL CYTOLOGY (1146)
 NASOPHARYNX
 CARCINOMA, BURKITT'S LYMPHOMA,
 EPSTEIN-BARR VIRUS (1024)
 ETHMOID ADENOCARCINOMA, WOOD DUST,
 FURNITURE INDUSTRY (0982)
 HEOCARZINOSTATIN
 BURKITT'S LYMPHOMA CELLS, EPSTEIN-BARR
 VIRUS, VIRUS (1020)
 NEOPLASM
 EPIDEMIOLOGY, REVIEW (0868)*
 RAT RETICULAR TUMOR, LETHAL YELLOW
 GENE, HEPATOMA (1198)
 NERVE
 TUMORS, RATS, N-METHYL-N-NITROSUREA
 (0965)
 NERVOUS SYSTEM
 NEURINOMA, LACTIC DEHYDROGENASE,
 ISOZYME, RATS (0966)
 TUMORS, ALDOLASE ISOZYME ACTIVITY
 (1255)
 TUMORS, ENZYME LEVELS (1196)
 NEUROBLASTOMA
 DNA REPLICATION, HUMAN (1230)
 MITOTIC INDEX, CELL PROLIFERATION
 (1242)
 NICKEL
 COBALT, OCCUPATIONAL EXPOSURE, CANCER
 INCIDENCE (1185)
 -NITROGUINOLINE-1-OXIDE
 DNA REPAIR SYNTHESIS, CHROMOSOME
 ANOMALY, HUMAN, HAMSTER (0968)
 METABOLISM, ELIMINATION, RAT (0967)
 ITOSAMINE
 SPINACH, CARCINOGENIC HYDROCARBONS
 (0860)*
 -NITROSODIETHYLAMINE
 HEPATOCARCINOMA, MONKEY,
 ULTRASTRUCTURE (0955)
 -NITROSODIMETHYLAMINE
 TUMORIGENESIS, MASTOMYS (0958)
 -NITROSO-N-METHYLUREA
 NEWBORN AND WEANED MICE, LYMPHOSARCOMA
 (0962)
 NUCLEIC ACID
 DISTRIBUTION, ASCITIC SARCOMA, ROUS
 SARCOMA VIRUS, MOUSE CELL (1080)
 MICROSOMAL MEMBRANE, LIVER, CHEMICAL
 CARCINOGEN, RAT (0913)
 MYCOTOXIN, HEPATIC CANCER (0849)
 SYNTHESIS, PHENOBARBITAL, AFLATOXIN B1
 (0919)
 TUMOR, VX7 TYPE CARCINOMA, SHOPE VIRUS
 PAPILLOMAS (1074)
 OCCUPATIONAL HAZARD
 BERYLLIUM, CHRONIC INTOXICATION,
 CANCER (0981)
 CARCINOMA OF THE SCROTUM, MINERAL OILS
 (0859)
 GLASS FIBERS, LUNG CANCER, REVIEW
 (0874)*
 INORGANIC AGENTS, AZO DYES, RADIATION,
 REVIEW (0878)*
 INORGANIC CARCINOGENS, RADIATIONS,
 REVIEW (0877)*
 RADIATION, QUARTZ, PLEURAL MESO-
 THELIOMA (0996)
 SCOTLAND, MESOTHELIOMA, ASBESTOS
 (1170)
 TUMORS OF URINARY BLADDER, TEXTILE
 WORKERS (0980)
 WOOD DUST, ETHMOID ADENOCARCINOMA,
 FURNITURE INDUSTRY (0982)
 ORAL CAVITY
 BUCCAL MUCOSA, TOBACCO CHEWING,
 BETEL-NUT (0978)
 HISTOLOGY OF BUCCAL MUCOSA, TOBACCO
 CHEWING, BETEL-NUT CHEWING (0979)
 ORAL AND OROPHARYNGEAL CANCER, INDIA,
 TOBACCO CHEWING (1177)
 SQUAMOUS CELL CARCINOMA, CANINE
 PAPILLOMATOSIS (1151)
 ORAL CONTRACEPTIVE
 MAMMARY CARCINOMA (0984)
 OVARY
 UTERUS, MAMMARY GLAND, CARCINOMA,
 IMMUNOLOGY (1135)
 OZONE
 LUNG, NEOPLASIA, MICE (0884)
 PANCREAS
 CANCER, DIABETES MELLITUS (1244)
 CANCER, MORTALITY RATES, CIGARETTE
 SMOKING (1178)
 HAMSTER ISLET CELL TUMORS, DOPA,
 TYROSINE HYDROXYLASE ACTIVITY (1222)
 PAPILLOMA
 CANINE, SQUAMOUS CELL CARCINOMA, ORAL
 CAVITY (1151)
 SHOPE VIRUS, VX7 TYPE CARCINOMA,
 NUCLEIC ACID (1074)
 PARATHYROID
 ADENOMA, ANNULATE LAMELLAE, MITO-
 CHONDRIA (1246)
 PATHOGENESIS
 AMERICUM 241, HISTOLOGICAL DISTRIBUTION
 IN RAT (1016)*
 LARYNX, ELECTRON MICROSCOPY, LIGHT
 MICROSCOPY (1152)
 NEOPLASM, ENZYME, MODIFICATION
 PROCESSES, REVIEW (0860)
 PRECANCEROUS STATE, ESOPHAGITIS,
 CICATRITION, PEPTIC STENOSIS (0851)
 UTERINE CARCINOMA, REVIEW (0852)
 PESTICIDES
 RENAL ADENOCARCINOMA, LEOPARD FROGS
 (0896)
 PETS
 DOMESTIC CATS, HUMAN LYMPHOMA, HOUSE-
 HOLD QUESTIONNAIRE SURVEY (1182)
 PHARYNX
 HYPOPHARYNX, CARCINOMA, RADIATION
 EXPOSURE (0995)
 PHENOBARBITAL
 AFLATOXIN B1, LIVER NUCLEIC ACID

- SYNTHESIS (0919)
- PHORBOL
LEUKEMOGENESIS, 7,12-DIMETHYLBENZ-(A)ANTHRACENE (0893)
15-C-TETRADECANOYL-PHORBOL-12-ACETATE, THYMIDINE INCORPORATION, CROTON OIL (0892)
- PHYTOHEMAGGLUTININ
HUMAN LYMPHOCYTE AGGREGATE ENZYME, RNA SYNTHESIS (1138)
LYMPHOCYTES, IMMUNITY (1137)
MITOTIC BLOCK, CELL DEATH, RADIATION (1136)
RAT LYMPH NODE CELLS, NONSPECIFIC ANTIBODY, SV40 (1097)
SPLEEN, THYMUS, LUNPH NODES (1122)
- PINGUECULA
AFRICAN PATIENTS, CONJUNCTIVAL LESIONS (1213)
- PLACENTA
3'-METHYL-4-DIMETHYLAMINOAZOBENZENE, PARTIAL HEPATECTOMY, RAT (0987)*
- POLYPS
GASTRIC MUCOSA, ADENOMATOUS (1155)
- PROLACTIN
GROWTH OF MAMMARY TUMORS, 7,12-DIMETHYLBENZ(A)ANTHRACENE (0927)
- PROLIFERATION
BONE MARROW, CHLORAMBUCIL, SERUM, RAT (0901)
- CHICKEN EMBRYO CELLS, ROUS SARCOMA VIRUS (1082)
FIBROBLASTIC, ACUTE MYELOFIBROSIS, CHROMOSOME ABNORMALITY (1247)
KINETICS, ACUTE LEUKEMIA, METHODS, REVIEW (0876)*
MITOTIC INDEX, NEUROBLASTOMA CELLS (1242)
ROUS SARCOMA VIRUS, CHICK EMBRYO CELL (1083)
- PROSTATE
BLUE NEVUS, MELANOCYTES (1239)
ESTROGEN, PROGESTERONE, DNA, RNA, RAT (0889)
HYPERPLASIA, ANDROGEN TREATMENT, PRAOMYS (MASTOMYS) NATALENSIS (0885)
- PROTEIN
BENZO(A)PYRENE, RNA, DNA, BINDING, METABOLISM (0941)
CARCINOGEN BINDING, THE "DROP OUT" THEORY, REVIEW (0833)
COMPONENTS, AVIAN MYELOBLASTOSIS VIRUS (1064)
GLYCOPROTEIN SYNTHESIS, POLYOMA VIRUS, HAMSTER KIDNEY (1114)
INTRAMOLECULAR MODIFICATION, KINETICS, CARCINOGENS, ROLE IN TRANSFORMATION PROCESSES (1162)
LAMBDA, MYELOMA, SERUM (1127)
STRUCTURAL VIRAL PROTEINS, KILHAM RAT VIRUS (1071)
SURFACE ANTIGENS, AVIAN TUMOR VIRUSES (1085)
SYNTHESIS, ECTOPIC HORMONE PRODUCTION BY MALIGNANT CELLS, POLYPEPTIDE
- HORMONE PRODUCTION, REVIEW (0832)
SYNTHESIS, FRIEND VIRUS, INFECTED SPLEEN CELLS (1032)
SYNTHESIS, MYELOMA CELL-LYMPHOMA CELL HYBRID, ANTIGEN (1124)
- PSEUDOVIRUS
SIMIAN, MOUSE EMBRYO CELLS, DNA (1094)
- RADIATION
ACUTE, THYMECTOMY, HEMATOPOIESIS, MICE (1001)
ALPHA PARTICLE IRRADIATION, FIBRO-SARCOMA, RAT (0992)
AMERICUM 241, HISTOLOGICAL DISTRIBUTION IN RAT, PATHOGENESIS (1016)*
BOMB IRRADIATION, TUMORIGENESIS, SWINE (0994)
CELL DEATH, MITOTIC BLOCK, PHYTOHEMAGGLUTININ (1136)
CERIUM 144, TISSUE DISTRIBUTION IN DOGS, ONCOGENICITY (1015)
EXPOSURE, HYPOPHARYNX, CARCINOMA (0995)
GAMETES, ZYGOTES, DROSOPHILA MELANOGASTER, CARCINOGENESIS (0998)
IONIZING, HUMAN BONE MARROW (0993)
LEUKEMOGENESIS, 7,12-DIMETHYLBENZ(A)ANTHRACENE, BONE MARROW CELLS (0928)
LYMPHOCYTE, CHROMOSOME, ABERRATION, HUMAN (1008)
NEUTRON IRRADIATION, PIG LEUKOCYTES, CHROMOSOME ABERRATIONS (1005)
NUCLEAR BOMB, GASTRIC CARCINOMA (1172)
PLUTONIUM, RETENTION IN BONE CELLS (1012)
239PU EXPOSURE, RISK OF TUMOR DEVELOPMENT (1003)
POTENTIATION OF TUMORIGENICITY, PASSAGE IN VITRO OF SV40 (1093)
PROTON-IRRADIATION, DEEP BRAIN LESION, HISTOPATHOLOGY (1007)
QUARTZ, SILICOSIS, PLEURAL MESOTHELIOMA (0996)
RADIUM EXPOSURE, CHILDREN, BONE CANCER INDUCTION (1000)
STRONTIUM 90, INHALATION OF 90SR BY DOGS, CARCINOGENICITY (1014)
STRONTIUM 90, RETENTION IN ORGANS, BEAGLE DOGS (1013)
SUNLIGHT, MALIGNANT MELANOMA (0835)
SUNLIGHT, MELANOMA, SOLAR CIRCULATING FACTOR (0861)
SUNLIGHT, SQUAMOUS CELL CARCINOMA OF SKIN, HAND AND ARM (0997)
SUPRA-LETHAL DOSE, CHANGES IN LUNG TISSUE (1009)
THORIUM 232, HUMAN BONE (1006)
THIOCTRAST, 131I-LIPIDOL (0845)
TUMORIGENESIS, RISK, RADIUM (0836)
- UV, BENZ(A)PYRENE, DNA, PHOTO ADDUCT (0938)
UV IRRADIATION, NON-PROLIFERATING ACUTE LEUKEMIA CELLS, DNA SYNTHESIS (1223)
X-IRRADIATION, MYXOVIRUS INFECTION, CHROMOSOME ABERRATIONS (1002)

X-IRRADIATION, SPLEEN IMMUNE RESPONSE, BURSECTOMY (1134)
 X-IRRADIATION, STEM CELL PROLIFERATION, BONE MARROW STEM CELLS (1011)
 X-RAY, LEUKEMIA, HYDROCORTISONE, MICE (0999)

RECTUM
 CARCINOMA, HEREDITARY DISTRIBUTION, FAMILIAL POLYPOSIS OF THE COLON (1245)

VILLOUS ADENOMA, ELECTROLYTE DISTURBANCE, POTASSIUM LOSS (1211)

DEGENERATION
 LIVER, MOUSE HEPATOMAS, URETHAN (0971)

ESERPINE
 7,12-DIMETHYLBENZ(A)ANTHRACENE, MAMMARY TUMOR (0929)

RESPIRATORY TRACT
 CARCINOMA OF THE TONSIL, URBAN AIR POLLUTION, CANINE (1183)

ETICULOENDOTHELIAL SYSTEM
 THOROTRAST, 131I-LIPIODOL, REVIEW (0845)

ETICULOPROLIFERATIVE DISEASE
 HERPESVIRUS SAIMIRI, VIRUS, RINGTAIL CINNAMON MONKEY (1059)

ETICULOSARCOMA
 CELL LINES IN HEMATOPOIETIC TISSUES, CYTOLOGIC STUDY (1224)

ETINOBLASTOMA
 IN VITRO CULTURE, MALIGNANT TRANSFORMATION (1234)

ABDOMYOSARCOMA
 DNA REPLICATION, HUMAN (1230)
 EPIDERMODYSPLASIA VERRUCIFORMIS, VIRUS-LIKE PARTICLES (1017)

RIBOFLAVIN
 DEFICIENCY, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, SKIN TUMORS (0935)

NA
 ARGINYL-TRNA, SERYL-TRNA, HUMAN EPIDERMAL CARCINOMA, HERPES SIMPLEX (1058)
 AVIAN SARCOMA VIRUS, NONTRANSFORMANT (1066)
 LYSYL-TRANSFER, DIETHYLSTILBESTEROL, CHICKEN LIVER (1205)
 MESSENGER, FREE, POLYRIBOSOME BOUND, HELA CELLS (1203)
 MURINE SARCOMA-LEUKEMIA, VIRUS (1076)
 POLYMERASE, MAMMALIAN, VIRUS, DNA (1103)
 7S, ROUS SARCOMA VIRUS (1088)
 SPLEEN, RAUSCHER VIRUS, MOUSE (1038)
 SYNTHESIS, HUMAN LYMPHOCYTE AGGREGATE ENZYME, PHYTOHEMAGGLUTININ (1138)
 SYNTHESIS, LIVER CELLS, AFLATOXIN B1 (0914)
 SYNTHESIS, TOYOCAMYCIN, VIRUS-INFECTED CHICK EMBRYO CELLS (1105)
 SYNTHESIS INHIBITION, HUMAN KIDNEY CELLS, H-1 VIRUS, VIRUS (1099)
 TRANSFER, LEUKEMIA, LYMPHOBLAST (1204)
 TRANSFER, METHYLASES, REVIEW (0831)
 TRANSFER, METHYLATION, NEOPLASIA, MICE (1200)

TRANSFORMED CELLS, AVIAN MYELOBLASTOSIS VIRUS, CHICKEN (1026)

SARCOMA
 ASCITIC, 3-METHYLCHOLANTHRENE, CYTOGENETICS, HAMSTER (1219)
 ASCITIC TUMOR, ROUS SARCOMA VIRUS, NUCLEIC ACID, MOUSE CELL (1080)
 FERRIDEXTRAN SPOFA, ANTIGENICITY, RAT (0900)
 METHYLCHOLANTHRENE, GUM ARABIC, BOVINE SERUM, GUINEA PIG (0946)
 RETICULUM CELL, VIRUS, MOUSE (1075)
 SNYDER-THEILEN FELINE, PROPAGATION IN HUMAN CELL CULTURES (1073)
 SUBCUTANEOUS, CADMIUM CHLORIDE, RAT (0898)
 YOSHIDA ASCITES, HORMONE, TUMOR GROWTH, OVARICTOMIZED RATS (1214)

SCAR TISSUE
 ESOPHAGEAL STENOSIS, CAUSTIC AGENTS, EPITHELIOMA, MAN (1154)
 SCLEROTIC FOCI, NEOPLASTIC TRANSFORMATION, LUNG (1153)

SCROTUM
 CARCINOMA, MINERAL OILS, OCCUPATIONAL EXPOSURE (0859)

SILICONE
 AUGMENTATION MAMMAPLASTY, BENIGN TUMOR INCIDENCE (0986)*

SKIN
 BENZO(A)PYRENE HYDROXYLASE, 3-METHYLCHOLANTHRENE, RAT (0939)
 CARCINOMA, TANZANIA, SQUAMOUS CELL CARCINOMA OF THE CERVIX (1176)
 DNA REPLICATION, 7,12-DIMETHYLBENZ(A)ANTHRACENE, MICE (0931)
 LIPIDS, LABELED ACETATE INCORPORATION, AFLATOXIN B1, HUMAN (0918)
 MOUSE SQUAMOUS EPITHELIUM, TOBACCO SMOKE CARCINOGENESIS, EXPERIMENTAL BIOASSAY SYSTEM (0977)
 SQUAMOUS CELL CARCINOMA, HAND, ARM, SUNLIGHT (0997)
 TUMORS, RIBOFLAVIN DEFICIENCY, 7,12-DIMETHYLBENZ(A)ANTHRACENE (0935)

SMOKED FOOD
 CARCINOGENESIS, REVIEW (0879)*

SPLEEN
 CELLS, FRIEND VIRUS, PROTEIN SYNTHESIS (1032)
 FRIEND VIRUS, LEUKEMIA (1022)
 IMMUNE RESPONSE, BURSECTOMY, X-IRRADIATION (1134)
 RNA, RAUSCHER VIRUS, MOUSE (1038)
 THYMUS, LYMPH NODES, PHYTOHEMAGGLUTININ (1122)

STOMACH
 CANCER, INDUCTION IN DIFFERENT REGION, 20-METHYLCHOLANTHRENE (0947)
 CANCER, SOY BEAN PASTE CONSUMPTION, KOREA (1174)
 GASTRIC CARCINOMA, MUCOSA, HISTOCHEMICAL STAINING PROPERTIES, HUMAN (1217)
 GASTRIC CARCINOMA, NUCLEAR BOMB RADIATION (1172)

- GASTRIC MUCOSA, GENESIS OF POLYP,
 ADENOMATOUS POLYP (1155)
 N-NITROSODIMETHYLAMINE, MASTOMYS
 (0958)
 SULTONES
 1,3-PROPANE SULTONE, 1,4-BUTANE
 SULTONE, NEUROGENIC TUMORS, RATS
 (0905)
 SURGERY
 GASTRIC, RECTAL CANCER, ESOPHAGEAL
 CANCER (1228)
 SUPPRESSION OF IMMUNOCOMPETENCE,
 CARCINOMA PATIENTS (1116)
 SYNDROME
 SEZARY, ATYPICAL LYMPHOID CELLS,
 PRELYMPHOMATOUS CONDITION (1206)
 TEMPERATURE
 EFFECT, DNA SYNTHESIS, THERMOSENSI-
 TIVE, SV40, VIRUS, MUTANT (1090)
 TESTES
 TESTICULAR TUMOR, MORTALITY, TREAT-
 MENT, MAN (1186)
 THIAMINE
 DIETARY BRACKEN FERN, DEVELOPMENT OF
 BLADDER TUMORS (0899)
 THIOACETAMIDE
 LIVER TUMORS, METABOLIC CHANGES (0970)
 LIVER TUMORS IN MICE (0969)
 THOROTRAST
 131I-LIPODOL, CARCINOGENIC EFFECTS,
 REVIEW (0845)
 THYMUS
 IMMUNOLOGY, LYMPHOCYTES, IRRADIATION
 (0842)
 LYMPHOID TISSUE ANTIGEN, LEUKEMIA,
 LYMPHOMA (1121)
 THYMECTOMY, ACUTE RADIATION, MICE
 (1001)
 THYROID
 CARCINOMA, CHILDREN, EPIDEMIOLOGY AND
 CLINICAL COURSE (1173)
 THYROIDITIS, 3-METHYLCHOLANTHRENE
 (0944)
 TOBACCO
 CHEWING, BUCCAL MUCOSA, BETEL-NUT
 (0978)
 CHEWING, HISTOLOGY OF BUCCAL MUCOSA,
 BETEL-NUT CHEWING (0979)
 CHEWING, ORAL AND OROPHARYNGEAL
 CANCER, INDIA (1177)
 CIGARETTE SMOKING, BLADDER CANCER,
 LOWER URINARY TRACT CANCER (0976)
 CIGARETTE SMOKING, CANCER OF THE
 PANCREAS, MORTALITY RATES (1178)
 FILTERED CIGARETTES, BRONCHIOLO-
 ALVEOLAR TUMORS IN DOGS (0973),
 (0974)
 SMOKE CARCINOGENESIS, EXPERIMENTAL
 BIOASSAY SYSTEM, MOUSE SQUAMOUS
 EPITHELIUM (0977)
 SMOKING, EPIDEMIOLOGY, CARCINOMA OF
 THE TONGUE (0847)
 SQUAMOUS CELL CARCINOMA OF THE HEAD
 AND NECK, ETIOLOGICAL FACTORS (0850)
 WOMEN CIGARETTE SMOKERS, RESPIRATORY
 FUNCTION, SPUTUM CYTOLOGY (0975)
 TONGUE
 CARCINOMA, EPIDEMIOLOGY, SMOKING
 (0847)
 TOYCAMYCIN
 VIRUS-INFECTED CHICK EMBRYO CELLS,
 RNA SYNTHESIS (1105)
 TRACHEA
 EPITHELIUM, VITAMIN A DEFICIENCY,
 METAPLASIA, RAT (1209)
 TRANSFORMATION
 ARGINASE, ANAEROBIC GLYCOLYSIS,
 EMBRYO CELLS (1143)
 DIMETHYLNITROSAMINE, REVERTANT,
 LIMITED LIFE-SPAN, HAMSTER EMBRYO
 CELL (0951)
 IN VITRO NEOPLASTIC, TUMORIGENICITY
 OF MOUSE CELL LINES (1229)
 LEUKEMIC, NORMAL MARROW CELL GRAFT
 (1201)
 MACROPHAGE, SV40 (1096)
 MALIGNANT, IN VITRO CULTURE OF RETINO-
 BLASTOMA, RETINOBLASTOMA (1234)
 MALIGNANT, LACRIMAL GLAND TUMOR (1149)
 MALIGNANT, METABOLIC CHANGES, PHASES
 OF CELL GROWTH (0854)
 NEWBORN HAMSTER CELL, CELL PROPERTIES,
 MORPHOLOGY, KARYOTYPE (1241)
 REVERSAL, TUMOR DNA (1210)
 ROUS VIRUS REPLICATION, GENOME
 SUBUNITS, CHICK EMBRYO FIBROBLASTS
 (1078)
 SV40, POLYOMA VIRUS, GANGLIOSIDE
 ALTERATION (1091)
 SV40, VARIANT, DNA, HUMAN FIBROBLAST
 (1095)
 TRANSPLANTATION
 FAT TISSUE, BREAST CANCER, HUMAN
 (1010)
 ORGAN, DEVELOPMENT OF MALIGNANCY,
 IMMUNOSUPPRESSIVE THERAPY (1118)
 ORGAN, INDUCED IMMUNOLOGIC INSUFFI-
 CIENCY, MALIGNANT (0839)
 TRICHOMONAS
 UTERINE CERVIX, CANCER (1265)*
 TRYPTOPHAN
 METABOLISM, 3-HYDROXYANTHRANILIC ACID,
 EARLY BENZIDINE CARCINOGENESIS, RAT
 (0911)
 ULTRASTRUCTURE
 CARDIAC MYXOMA (1253)
 EPIDIDYMUS, MESOTHELIAL ORIGIN OF
 TUMOR, ADENOMATOID TUMOR (1161)
 GLOMUS TUMOR, EPITHELIOID CELLS,
 HISTOGENESIS (1227)
 HEPATOCARCINOMA, MONKEY, N-NITROSO-
 DIETHYLAMINE (0955)
 HISTOPATHOLOGY, DEEP BRAIN LESIONS,
 PROTON-IRRADIATION (1007)
 HUMAN GASTRIC MUCOSA, CARCINOMA,
 HISTOCHEMICAL STAINING PROPERTIES
 (1217)
 KERATINOCYTE, SQUAMOUS CELL CARCINOMA,
 DESMOSOMES, HUMANS (1231)
 LARYNX, PRECANCEROUS CHANGES, CHRONIC
 LARYNGITIS (1152)
 LEUKEMIA, GRAFFI VIRUS, MICE (1040)
 URETHAN
 CARCINOGENICITY, ENHANCED DETECTION,

* indicates a plain citation without accompanying abstract

TRANSPLACENTAL EFFECTS, MOUSE (0972)
 MOUSE HEPATOMAS, REGENERATION, MOUSE (0971)
 UROGENITAL TUMOR
 LOWER, BLADDER CANCER, CIGARETTE SMOKING (0976)
 UTERUS
 CARCINOMA, PATHOGENESIS, REVIEW (0852)
 CHANGES, ESTROGEN TREATMENT, INTRA-UTERINE CONTRACEPTIVE DEVICE, RAT (0985)
 GONADAL DYSGENESIS, XY SEX CHROMOSOME, AMENORRHEA, MALIGNANCY (1261)
 VAGINA
 GENITAL INFECTION IN CEBUS MONKEY, HERPESVIRUS HOMINIS (1061)
 VIRUS
 ADENOVIRUS, CANAVANINE, INHIBITION OF REPLICATION (1046)
 ADENOVIRUS, CAPSID PROTEINS (1043)
 ADENOVIRUS, DNA SYNTHESIS, HAMSTER KIDNEY CELL, HUMAN EMBRYO LUNG CELL (1044)
 ADENOVIRUS, MAGNESIUM CHLORIDE, ENHANCED PLAQUE FORMATION, (1053)
 ADENOVIRUS ASSOCIATED VIRUS, ENHANCEMENT, HERPES SIMPLEX VIRUS (1056)
 ADENOVIRUS TYPE 2, SV40, HYBRID, DNA (1052)
 ADENOVIRUS TYPE 8, TYPE 9, IMMUNOLOGY (1054)
 ADENOVIRUS TYPE 12, ACTIVATION OF DNA SYNTHESIS IN HAMSTER CELLS (1047)
 ADENOVIRUS TYPE 12, DNA, KIDNEY CELLS (1051)
 ADENOVIRUS TYPE 12, TRNA METHYLASE, HAMSTER (1049)
 ADENOVIRUS TYPE 12, TUMOR CELL EXTRACTS, TRANSPLANTATION IMMUNITY (1055)
 ADENOVIRUS TYPE 12, 6, 3, RAT EMBRYO FIBROBLASTS, GLYCOLYSIS (1048)
 AVIAN LEUKOSIS, ROUS SARCOMA, IMMUNOLOGIC CROSS-REACTION, GROUP SPECIFIC ANTIGEN, HUMAN LEUKEMIC PLASMA (1126)
 AVIAN MYELOBLASTOSIS, ANTIGEN, AMINO ACID (1027)
 AVIAN MYELOBLASTOSIS, ANTIGENICITY (1065)
 AVIAN MYELOBLASTOSIS, POLYRIBOSOMES, RNA, CHICKEN (1026)
 AVIAN MYELOBLASTOSIS, PROTEIN COMPONENTS (1064)
 AVIAN SARCOMA, NONTRANSFORMANTS, RNA DIFFERENCES (1066)
 AVIAN TUMOR, PROTEIN COMPONENTS, SURFACE ANTIGENS (1085)
 AVIAN TUMOR, TOYOCAMYCIN, CHICK EMBRYO CELLS, RNA SYNTHESIS (1105)
 BURKITT'S LYMPHOMA, INCIDENCE, REVIEW (0870)*
 CHROMOSOME ABERRATIONS, VIRAL INDUCTION (0866)*
 COMMON ANTIGEN, MAREK'S DISEASE
 HERPES, EPSTEIN-BARR (1028)

DNA VIRUS-INDUCED ANIMAL TUMORS, HUMAN MAMMARY CARCINOMA, TUMOR-SPECIFIC NEOANTIGEN (1131)
 EFFECT ON IMMUNE SYSTEM, RETICULOENDOTHELIAL SYSTEM (0862)*
 EPSTEIN-BARR, ANTIBODY TITERS, HODGKIN'S DISEASE (1025)
 EPSTEIN-BARR, ANTIGEN, CLONED HUMAN LEUCOCYTES (1021)
 EPSTEIN-BARR, BURKITT'S LYMPHOMA, NASOPHARYNGEAL CARCINOMA (1024)
 EPSTEIN-BARR, BURKITT'S LYMPHOMA CELLS, NEOCARZINOSTATIN (1020)
 EPSTEIN-BARR, LYMPHOMA, INFECTIOUS MONONUCLEOSIS (0875)*
 FRIEND, SPLEEN CELLS, PROTEIN SYNTHESIS (1032)
 FRIEND LEUKEMIA, ERYTHROCYTES, OSMOTIC FRAGILITY (1033)
 FRIEND LEUKEMIA, SPLEEN, LEUKEMIA (1022)
 GRAFFI, MYELOGENOUS LEUKEMIA, ULTRA-STRUCTURE, MOUSE (1040)
 GROSS, ANTITHYMOCYTE SERUM, LYMPHOMA INCIDENCE (1035)
 GROSS LEUKEMIA, ANTIBODIES, GLOMERULONEPHRITIS, MOUSE (1034)
 GROSS LEUKEMIA, IMMUNOFLUORESCENT FOCUS ASSAY, ANTIBODY (1036)
 GUINEA PIG, LEUKEMIA (1039)
 H-1, RNA SYNTHESIS INHIBITION, HUMAN KIDNEY CELLS (1099)
 HERPES, MAREK'S DISEASE, EPSTEIN-BARR, ANTIBODY, HUMAN SERA (1063)
 HERPES, VIRAL ANTIGENS ON CELL MEMBRANES (1062)
 HERPES SIMPLEX, ARGINYL-TRNA, SERYL-TRNA, HUMAN EPIDERMAL CARCINOMA (1058)
 HERPES SIMPLEX, TEMPERATURE-SENSITIVE MUTANT (1060)
 HERPES-TYPE, MAREK'S DISEASE (1031)
 HERPES-TYPE, MAREK'S DISEASE, CYTOPATHIC AGENT (1030)
 HERPES-TYPE, PROPAGATION, PROPERTIES, MAREK'S DISEASE (1029)
 HERPESVIRUS HOMINIS, GENITAL INFECTION IN CEBUS MONKEY (1061)
 HERPESVIRUS SAIRI, RETICULOPROLIFERATIVE DISEASE, RINGTAIL CINNAMON MONKEY (1059)
 HUMAN ADENO TYPE 12, SARCOMA, ANTIGEN, HAMSTER (1050)
 HUMAN ADENOVIRUS TYPE 12, CHICKEN LEUKOCYTES, INTERFERON PRODUCTION (1045)
 HUMAN LYMPHOBLASTS, EPSTEIN-BARR, INFECTIVITY AND CYTOPATHOLOGY (1023)
 ISOLATION OF NEW VIRUS, AVIAN TUMOR VIRUSES, CHICK EMBRYO FACTOR (1086)
 KILHAM RAT, STRUCTURAL PROTEINS (1071)
 LARGE AND SMALL PLAQUE VARIANTS, VIRULENCE, HERPES (1057)
 LEUKEMIA, MAN, REVIEW (0867)*
 MAMMARY TUMOR, MILK (1067)
 MOLONEY LEUKEMIA, LYMPHOMA, MURINE

(1077)
 MOLONEY SARCOMA, RESCUE, VIRUS CARRIER
 CELL LINE, HAMSTER TUMOR CELL (1070)
 MURINE LEUKEMIA, POLYINOSINIC-
 POLYCYTIDYLIC ACID, INTERFERON,
 EMBRYO CELLS (0953)
 MURINE LEUKEMIA, PLAQUE ASSAY TECH-
 NIQUE (1115)*
 MURINE SARCOMA, CELL TRANSFORMATION,
 MULTIPLICATION (1068)
 MURINE SARCOMA, LEUKEMIA, RNA (1076)
 MURINE SARCOMA (MOLONEY), GUAROA,
 ENHANCEMENT, MICE (1069)
 MYXOVIRUS INFECTION, X-IRRADIATION,
 CHROMOSOME ABERRATIONS (1002)
 ONCOGENIC RNA, BIOLOGICAL PROPERTIES,
 BIOCHEMICAL PROPERTIES (0837)
 PASSAGE IN VITRO OF SV40, POTENTIAL-
 TION OF TUMORIGENICITY (1093)
 POLYKARYOCYTOSIS, CELL FUSION (1019)
 POLYOMA, ANTIGENIC DIFFERENCES,
 IMMUNOCHEMICAL ANALYSIS (1107)
 POLYOMA, ARGININE DEPRIVATION, MOUSE
 EMBRYO CULTURES (1112)
 POLYOMA, DNA, THERMOSENSITIVE MUTANT
 (1109)
 POLYOMA, DNA SYNTHESIS, CYCLOHEXIMIDE,
 MOUSE EMBRYO CELL (1110)
 POLYOMA, DNA SYNTHESIS, MOUSE EMBRYO
 CELL (1106)
 POLYOMA, GLYCOPROTEIN SYNTHESIS,
 HAMSTER KIDNEY CELLS (1114)
 POLYOMA, IMMUNE RESPONSE TO TUMORS
 (1113)
 POLYOMA, IMMUNOSUPPRESSION, RESTORA-
 TION OF IMMUNOCOMPETENCE (1117)
 POLYOMA, MOUSE EMBRYO FIBROBLAST,
 VIRUS-DNA COMPLEX FORMATION (1111)
 POLYOMA, SARCOMA, PROTEIN SYNTHESIS
 (1108)
 POLYOMA, TRANSFORMED MOUSE CELLS,
 IMMUNE SERUM (1104)
 RAUSCHER, RNA, SPLEEN, MOUSE (1038)
 RAUSCHER LEUKEMIA, MAGNESIUM ACETATE,
 MANGANESE ACETATE (1037)
 RETICULUM CELL SARCOMA, MOUSE (1075)
 ROUS, GENOME SUBUNITS, TRANSFORMATION,
 CHICK EMBRYO FIBROBLASTS (1078)
 ROUS, POLYOMA, CELL TRANSFORMATION,
 ULTRASTRUCTURE, AMP (1079)
 ROUS SARCOMA, ASCITIC SARCOMA, NUCLEIC
 ACID, MOUSE CELL (1080)
 ROUS SARCOMA, AVIAN MYELOBLASTOSIS,
 DNA POLYMERASE (1081)
 ROUS SARCOMA, METASTASIS, CHROMOSOME,
 RAT (1084)
 ROUS SARCOMA, PROLIFERATION, CHICKEN
 EMBRYO CELLS (1082), (1083)
 ROUS SARCOMA, 7S VIRAL RNA (1088)
 ROUS SARCOMA, VARIANT STRAIN,
 TUMORIGENICITY FOR MAMMALS (1087)
 SHOPE, VX7 TYPE CARCINOMA, PAPILLOMAS,
 NUCLEIC ACID (1074)
 SNYDER-THEILEN FELINE SARCOMA, FILTER-
 ABLE AGENT, HUMAN CELL CULTURES
 (1073)

SV40, DEFECTIVE, ANTIGENIC RESPONSE
 (1100)
 SV40, DNA SYNTHESIS, HAMSTER (1089)
 SV40, HUMAN ADENOVIRUS TYPE 16,
 SENDAI, IMMUNOSUPPRESSION, HAMSTER
 (1042)
 SV40, LENGTH OF VIRAL DNA MOLECULE,
 INFECTIVITY (1098)
 SV40, MAMMALIAN RNA POLYMERASE, DNA
 (1103)
 SV40, MOUSE PERITONEAL MACROPHAGE,
 TRANSFORMATION (1096)
 SV40, PHYTOHEMAGGLUTININ, RAT LYMPH
 NODE CELLS, NONSPECIFIC ANTIBODY
 (1097)
 SV40, POLYOMA, FIBROBLASTS, GLYCOLIPID
 (1102)
 SV40, POLYOMA, GANGLIOSIDE ALTERATION
 (1091)
 SV40, SUPERINFECTION, POLYOMA, MOUSE
 FIBROBLASTS (1092)
 SV40, THERMOSENSITIVE SV40 MUTANT,
 DNA (1090)
 SV40, VARIANTS, DNA TRANSFORMATION,
 HUMAN FIBROBLAST CELL (1095)
 TUMORS, TUMOR ANTIGENICITY (0843)
 TYPE C, GLIOMA, HUMAN (1018)
 VIRAL ETIOLOGY FOR "SPONTANEOUS,"
 TRANSFORMATION, MOUSE EMBRYO FIBRO-
 BLAST CULTURE (1072)
 VIRAL GENETIC MATERIAL, LETHAL MUTA-
 TION (0864)*
 VIRUS-LIKE PARTICLES, RHABDOMYOSAR-
 COMA, EPIDERMODYSPLASIA VERRUCI-
 FORMIS (1017)
 WILM'S TUMOR
 CLINICAL FEATURES, CHILDHOOD CANCER
 (1180)
 ZINC
 DEFICIENCY, INHIBITION OF TUMOR
 GROWTH, WALKER 256 CARCINOSARCOMA
 (1232)



U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

OFFICIAL BUSINESS

PENALTY FOR PRIVATE USE, \$300

If you do not desire to continue receiving this publication, please CHECK HERE ☐;
tear off this label and return it to the above address. Your name will then be
promptly removed from the appropriate mailing list.

7405
R

*Vet.
Med.*

JANUARY-FEBRUARY 1971

Abstract Nos. 1267-1722

**Vol. 9
No. 7-8**

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health



CARCINOGENESIS ABSTRACTS

A monthly publication of the

National Cancer Institute

Editor

Robert Love, M.D.
Jefferson Medical College, Philadelphia

Associate Editor

George P. Studzinski, M.D.
Jefferson Medical College, Philadelphia

NCI Staff Consultants

Howard R. Rosenberg, M.S.
Sidney Siegel, Ph.D.
Elizabeth Weisberger, Ph.D.

THE LIBRARY OF THE
SEP 23 1971
UNIVERSITY OF ILLINOIS
AT URBANA-CHAMPAIGN

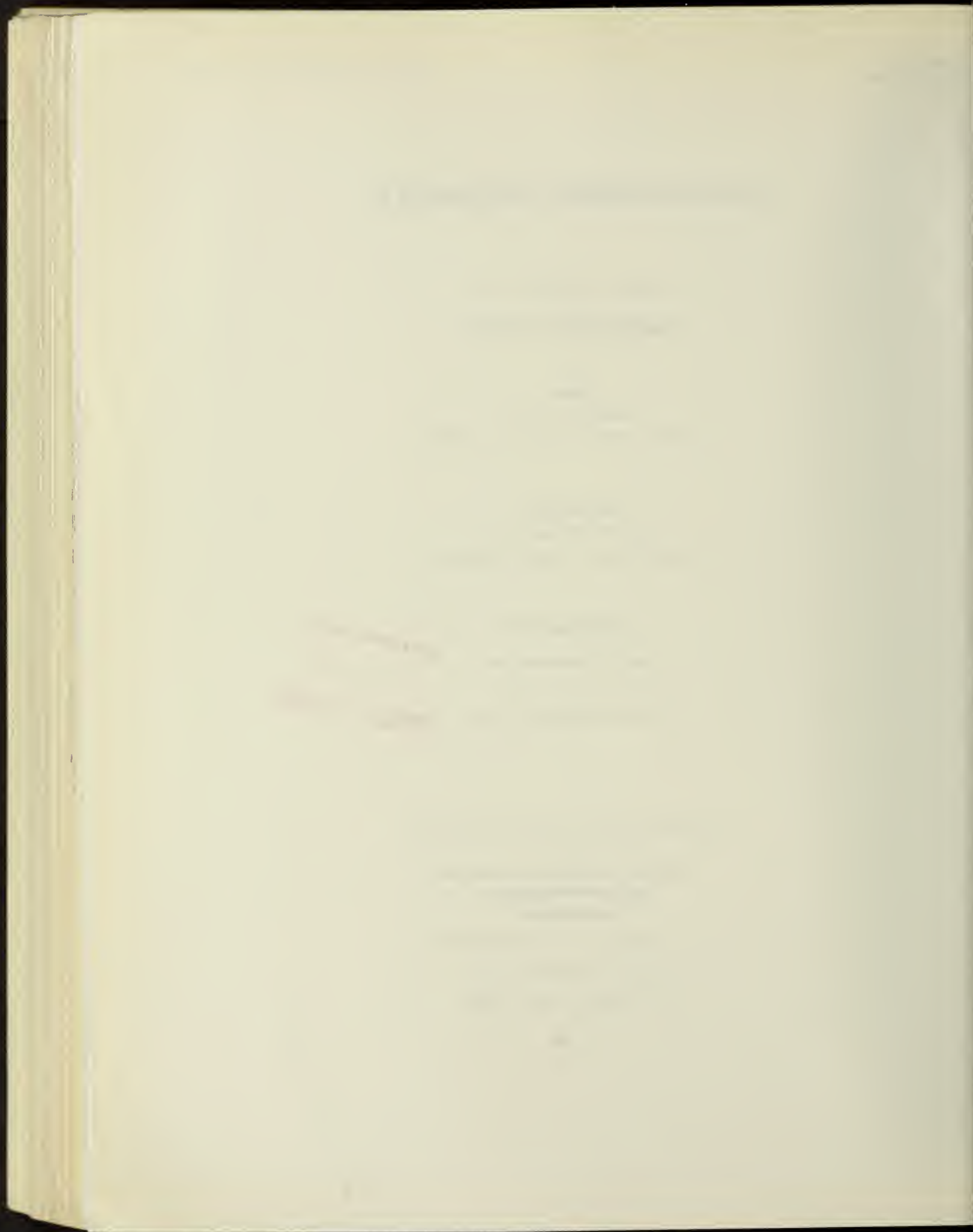
Literature Selected, Abstracted, and Indexed
by

The Franklin Institute Research Laboratories
Science Information Services
Biomedical Section

M. H. Fukami, Ph.D., Technical Editor

Contract Number NIH-71-2073

Public Health Service, USDHEW



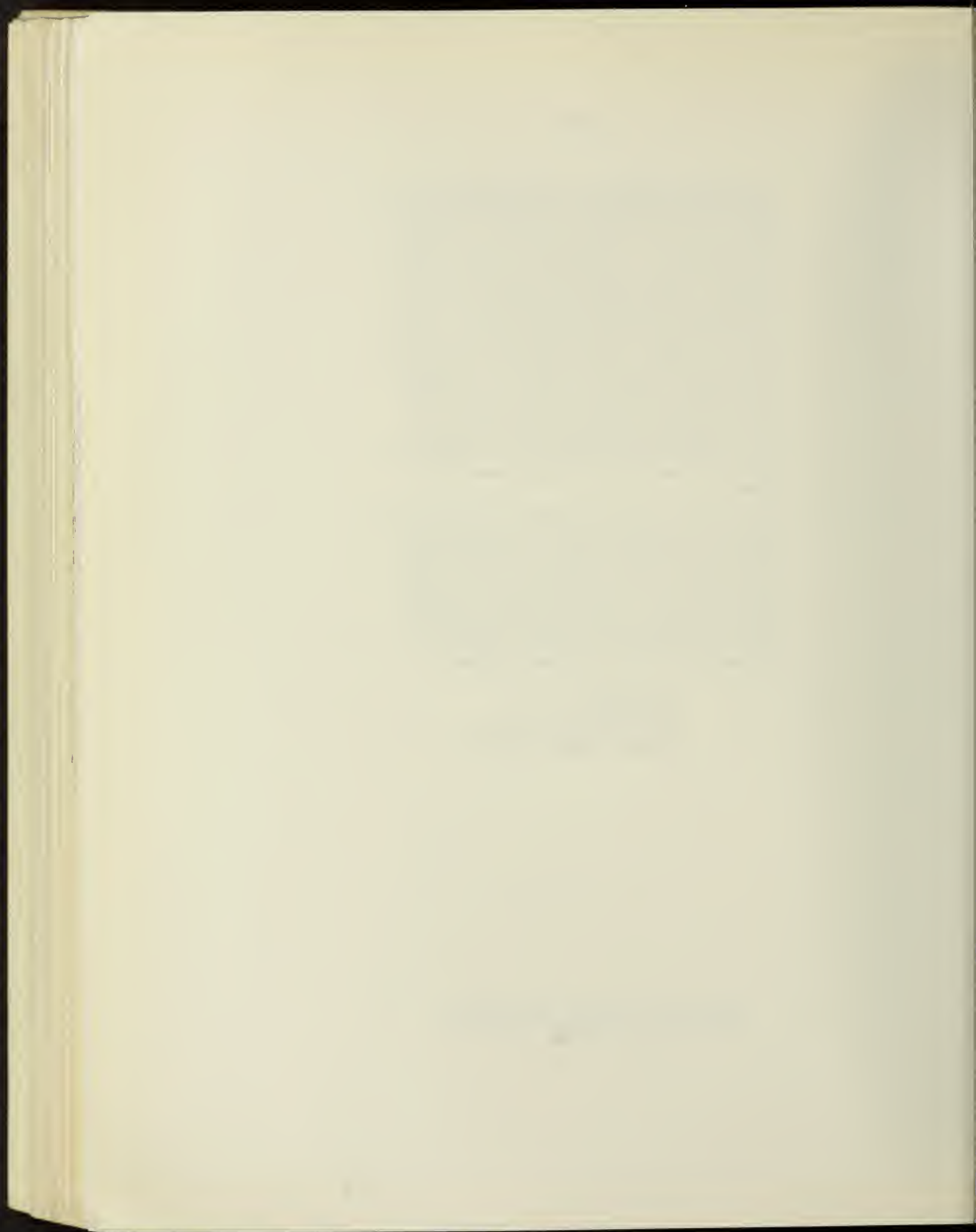
PREFACE

Carcinogenesis Abstracts is a publication of the National Cancer Institute. The journal serves as a vehicle through which current documentation of carcinogenesis research highlights are compiled, condensed, and disseminated on a regular basis. It represents an integral part of the Institute's program of fostering and supporting coordinated research into cancer etiology. Issues of *Carcinogenesis Abstracts* normally contain two-hundred abstracts and twenty citations (unaccompanied by corresponding abstracts). Abstracts and citations refer to the current scientific literature that describes the most significant carcinogenesis research carried on at the National Cancer Institute, other governmental agencies, and private institutions. *Carcinogenesis Abstracts* is intended to be a highly useful current awareness tool for scientists engaged in carcinogenesis research or related areas. The great number and diversity of publications relevant to carcinogenesis make imperative the availability of this service to investigators whose work requires that they keep abreast with current developments in the field.

Carcinogenesis Abstracts is normally published monthly. Volume IX covers the scientific literature published from July 1970 through June 1971. A cumulative subject and author index for Volume IX will be published shortly after the final regular issue. This journal is available free of charge to libraries and to individuals who have a professional interest in carcinogenesis. Requests for *Carcinogenesis Abstracts* from qualified individuals should include statements of their relationship to carcinogenesis research. All correspondence should be addressed as follows:

Carcinogenesis Abstracts
Etiology Area
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20014

Use of Funds for Printing this publication
approved by the Director of the Bureau of
the Budget on July 25, 1967.



NOTE

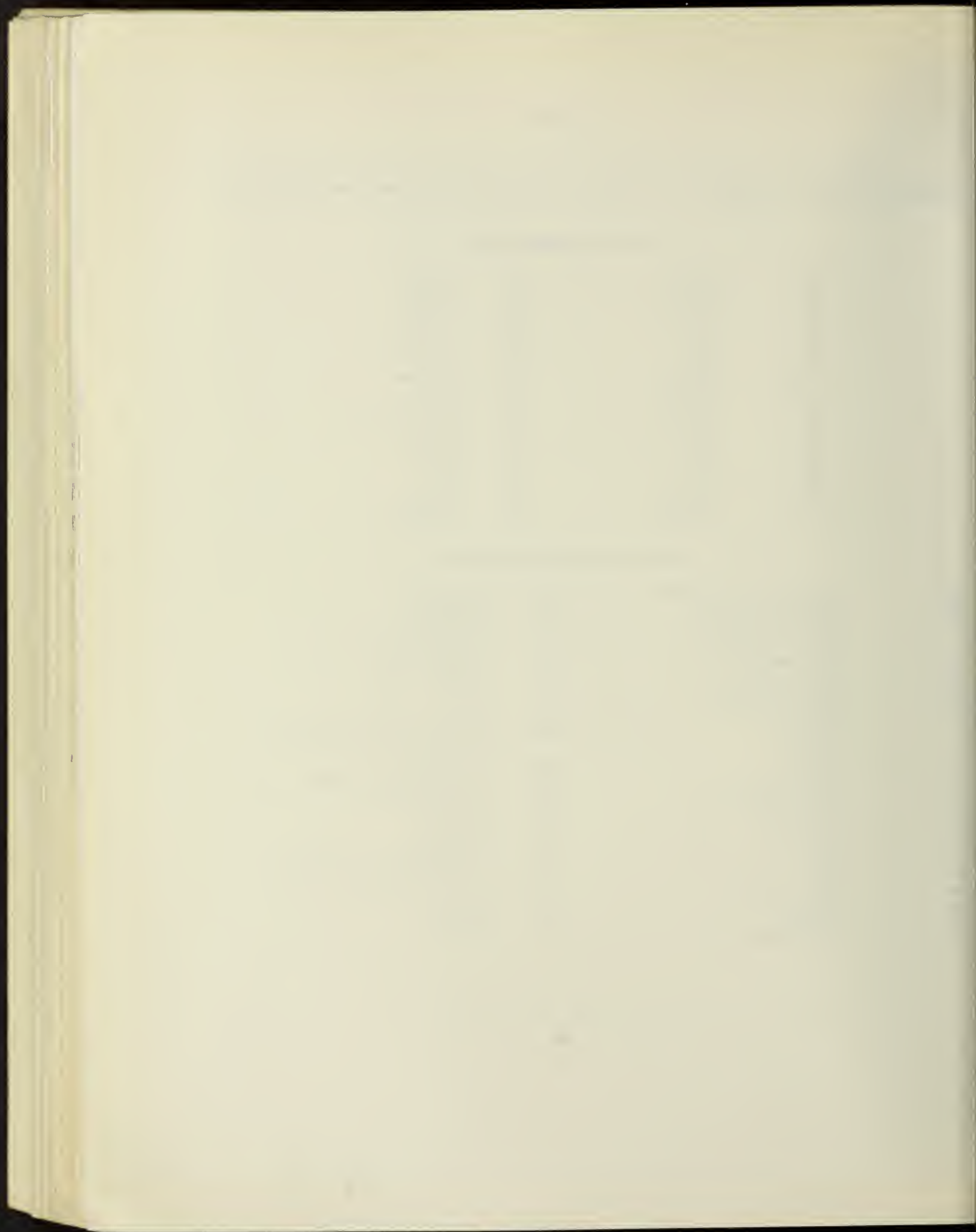
Journal names are abbreviated according to the list of abbreviations used by *Index Medicus*. For journals not covered by *Index Medicus*, the abbreviations (with some modifications) found in *World Medical Periodicals*, 3rd Edition, are used.

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	It.	Italian
Ar.	Arabic	Jap.	Japanese
Bul.	Bulgarian	Kor.	Korean
Ch.	Chinese	Latv.	Latvian
Cz.	Czech	Lith.	Lithuanian
Dan.	Danish	Nor.	Norwegian
Dut.	Dutch	Pol.	Polish
E.	English	Por.	Portuguese
Eston.	Estonian	Rum.	Rumanian
Fin.	Finnish	Rus.	Russian
Fl.	Flemish	Ser.	Serbo-Croatian
Fr.	French	Sl.	Slovak
Ger.	German	Sp.	Spanish
Gr.	Greek	Sw.	Swedish
Heb.	Hebrew	Th.	Thai
Hun.	Hungarian	Turk.	Turkish
Ic.	Icelandic	Uk.	Ukrainian
ln.	Indonesian	Viet.	Vietnamese

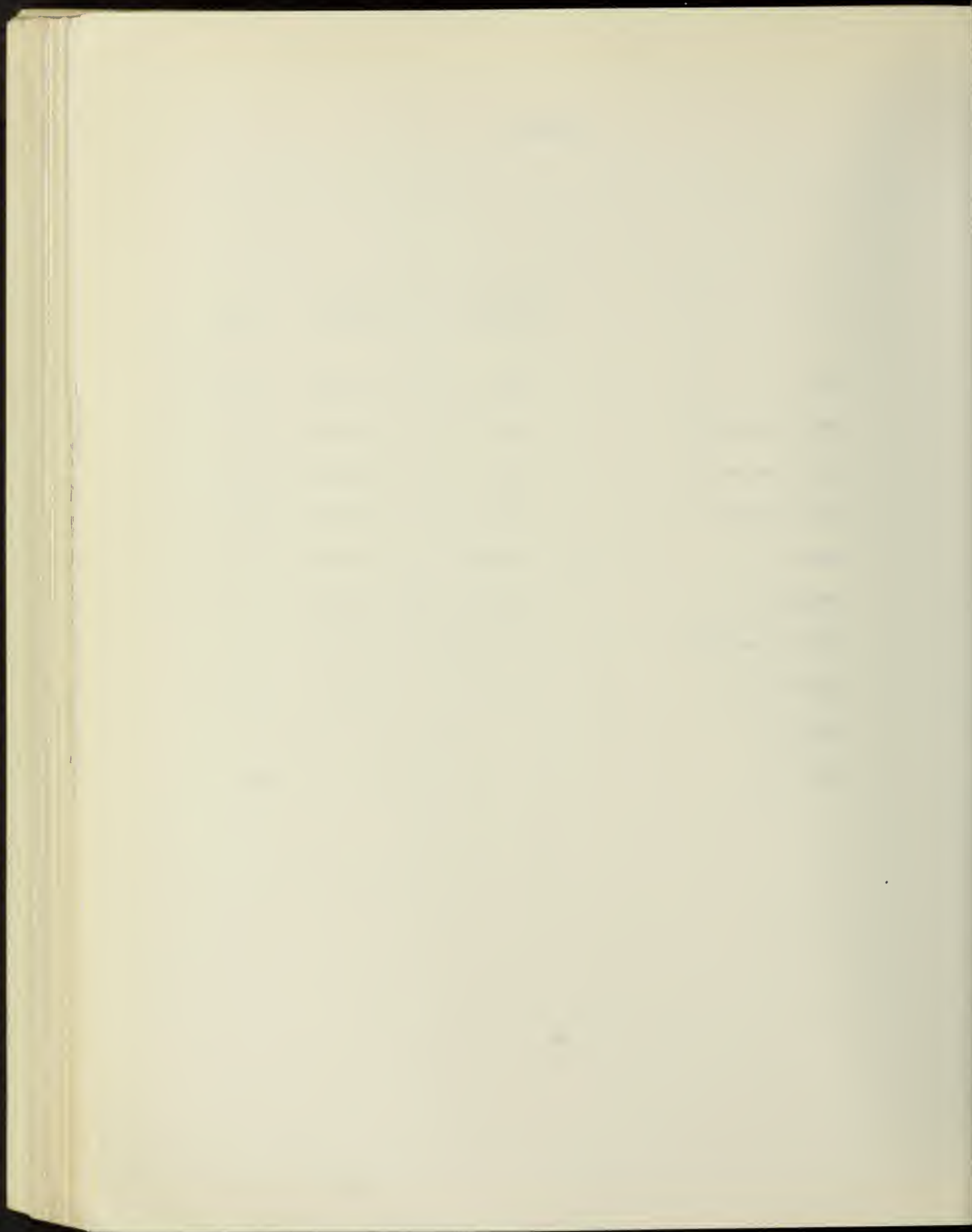
ABBREVIATIONS USED IN ABSTRACTS

ACTH	adrenocorticotrophic hormone	mg	milligram(s)
ADP	adenosine diphosphate	min	minute(s)
AMP	adenosine monophosphate	ml	milliliter(s)
ATP	adenosine triphosphate	mm	millimeter(s)
C	degrees centigrade	MTD	maximum tolerated dose
cm	centimeter(s)	ng	nanogram (10^{-9})
CNS	central nervous system	pg	picogram (10^{-12})
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	ppm	parts per million
e.g.	for example	r	Roentgen
g	gram(s)	RBC	red blood cells (erythrocytes), red blood count
µg	microgram(s)	resp.	respectively
hr	hour(s)	Rev.	review (only in citations)
i.m.	intramuscular	RNA	ribonucleic acid
i.p.	intraperitoneal	s.c.	subcutaneous
IU	international unit(s)	sec	second(s)
i.v.	intravenous	U	unit(s)
kg	kilogram(s)	UV	ultraviolet
LD ₅₀	median lethal dose(s)	WBC	white blood cells (leukocytes), white blood count
m	meter(s)	wk	week
M	molar	wt	weight
mEq	milliequivalent(s)	yr	year(s)
mM	millimolar		
µM	micromolar		
mC, µC	milli-,microcurie(s)		



CONTENTS

	Cross Reference Abbreviations	Abstracts, Citations	Page
REVIEW	(Rev)	1267-1286	277
CHEMICAL CARCINOGENESIS.	(Chem).	1287-1378	282
PHYSICAL CARCINOGENESIS.	(Phys).	1379-1410	303
VIRAL CARCINOGENESIS	(Viral)	1411-1518	309
IMMUNOLOGY	(Immun)	1519-1583	334
PATHOGENESIS	(Path).	1584-1601	350
EPIDEMIOLOGY AND BIOMETRY.	(Epid-Biom)	1602-1634	354
MISCELLANEOUS.	(Misc).	1635-1722	361
AUTHOR INDEX			i
SUBJECT INDEX.			xiii



REVIEW

- 1267 ON THE PROBABLE ROLE OF ONCOGENIC VIRUSES IN HUMAN EPIDEMIOLOGY. (E.) Clemmesen, J. (Danish Cancer Registry, Copenhagen). *Rev Europ Etud Clin Biol* 15(9):934-937, 1970.

Evidence for a viral etiology in human malignant diseases was reviewed. Human epidemiology has historically given little support to the hypothesis of a viral factor for human cancer. Microepidemics, familial cancer cases, and cancer occurring in a single dwelling place were not convincing on statistical analysis. A stronger argument for a viral genesis for neoplasia is that viral oncogenesis is clear for animals, and that no relevant dissimilarities have been thought to exist which distinguish men from animals in point of susceptibility to infection. However, it seems that some significant differences do exist between human and animal populations which might explain the presence in the latter of viral oncogenesis and its absence in the former. Among these differences is the prevalence of inbreeding in animal populations, and its rarity in human populations; reduced immunocompetence in inbred populations might explain the occurrence of viral infections of epidemic proportions. The exposure to chemical carcinogens in urban air, tobacco smoke, and industrial processes represents another feature distinguishing human and animal populations. Hygiene, moreover, has developed only in human populations. Recent evidence has shown that epidemics of malignant neoplasia have occurred in Africa (Burkitt's lymphoma) and among Chinese in Southeast Asia (nasopharyngeal carcinoma); viruses have been implicated in both these conditions. Whether virus transference from person to person is decisive in the genesis of these diseases, or whether viral infection is only a contributing factor for oncogenesis is uncertain. (24 references)

- 1268 THE PROTOVIRUS HYPOTHESIS: SPECULATIONS ON THE SIGNIFICANCE OF RNA-DIRECTED DNA SYNTHESIS FOR NORMAL DEVELOPMENT AND FOR CARCINOGENESIS. (E.) Temin, H. M. (McArdle Lab., U. Wisconsin, Madison). *J Nat Cancer Inst* 46(2):III-VII, 1971.

The provirus hypothesis suggests that "instructions" for neoplastic transformation may be transmitted vertically from cell to cell despite the fact that the original germ cell does not have these instructions encoded on its DNA; the mechanism for this transmission according to the provirus hypothesis is RNA-directed DNA synthesis which allows for changes in the DNA of cells without a random mutation having occurred. In normal cell development, RNA dependent DNA polymerase might bring about alteration of cells by causing the production of new DNA in one cell by RNA transferred to that cell from another; the combination of new and preexisting DNA in the former cell would promote variability in progeny cells. The usual process leading to neoplastic growth could be a variation in the normal physiological evolution of new DNA as a result of RNA-dependent DNA synthesis. The initial change in cell DNA leading to the transmission of instructions for neoplastic transformation might come about as a result of a virus, a chemical, or a physical stimulus applied to the cell. Transmission of these instructions might then proceed by means of DNA produced in

cells by RNA transferred to them from the original cell containing the instructions for cancerous change. (18 references)

- 1269 UNIFIED THEORY ON THE BASIC MECHANISM OF NORMAL MITOTIC CONTROL AND ONCOGENESIS. (E.) Cone, C. D., Jr. (Langley Res. Ctr., Hampton, Va.). *J Theor Biol* 30(1):151-181, 1971.

Results of an investigation of a fundamental mechanism for natural mitotic control associated with intracellular ionic balance and its effect on membrane potential difference were formulated into a theory of cytogenetic etiology and maintenance of the malignant state. There appears to be a positive correlation between the degree of mitotic activity of somatic cells and transmembrane potential level; large potential gradients within the cell membrane may have indirect secondary effects on intracellular conditions by producing steric modifications of the cell surface structure, resulting in alteration of membrane permeabilities for various ionic and molecular species. Since DNA synthesis is an essential prerequisite for normal mitosis, intracellular ionic environments associated with a given membrane potential level could act to regulate various osmotically associated aspects of metabolism connected with DNA synthesis through regulation of mRNA transcription or by activation or repression of the activity of already-formed enzymes. A proposed system of feedback interactions is feasible in which intracellular ion concentrations associated with the membrane potential act to influence cellular metabolic activity governing DNA synthesis, surface polymer production and mitochondrial activity; the latter two activities in turn may feed back to determine membrane potential levels. Since a number of oncogenic viruses exist which produce surface antigenic changes in somatic cells which are transformed, it is possible that their oncogenic action is entirely due to alteration or redirection of surface-associated polymer metabolism affecting membrane potential levels and allowing for increased mitotic activity. The closeness to which cell surfaces can approach and the tenacity with which they bond depend almost entirely upon the nature and specificity of the surface polymers. The modified antigenicity of malignant cell surfaces may be due to a stable alteration of the surface polymer preventing bonding between cells with consequent invasiveness and metastasis. Experimental data suggest increased sodium concentrations in excess of those normally used in tissue culture media show pronounced stimulatory mitotic effect, and trypsin which acts upon cell surface has produced acceleration of mitotic activity. The primary theoretical concept of mitogenic control which is proposed is based on experimental observations that a correlation exists between the electrical transmembrane potential level and the degree of mitotic activity for a substantial range of somatic cell types. (57 references)

- 1270 MITOCHONDRIAL DNA OF MALIGNANT CELLS. (Fr.) Paoletti, C. (Inst. Gustave Roussy, Villejuif, France) and G. Riou. *Bull Cancer* 57(3):301-334, 1970.

A characteristic structure in the mitochondrial DNA oligomer molecules has been described for malignant tumors which are invariably found in the white cells of chronic and acute myeloid and lymphoid leukemias; such structures were absent in normal white cells or in the benign hyperplasias. The modifications in the structure appear particularly in the length of the monocircular molecules, which suggests that this phenomenon may be due to an impairment of molecular mechanisms governing the synthesis of circular forms. The sequence of the base pairs in these abnormal oligomers, however, are similar to those in normal monomers, although one cannot exclude the existence of modifications, such as mutations, small zones of deletion or insertion, and methylation of the bases, etc. These data should be examined in the light of recent developments concerning the flotation density of mitochondrial DNA, which has been shown to differ in different species. The mechanism which may precipitate neoplastic tissue due to mitochondrial changes in DNA is discussed. (78 references)

- 1271 MORPHOLOGICAL ALTERATIONS OF THE THYMUS IN CANCER. (Rus.) Ageyev, A. K. (S. M. Kirov Acad. Med. Sci. Leningrad, U.S.S.R.). *Vop Onkol* 16(11):3-7, 1970.

A review of experimental data on the effect of thymectomy in very young animals on the enhanced development of tumors induced by viral or chemical agents is presented along with morphological data on thymic alterations detected in a series of patients who died of cancer. Of 28 patients 36-70 yr of age who died of lung, stomach, colon, pancreas, liver, uterine or mammary gland cancer, 21 had a decreased content of thymic parenchyma ranging from 0.5 to 6 g. The most distinct atrophic changes were noticed in patients who died between 36 and 55 yr-of-age; these alterations consisted in a considerable decrease in lymphocytes and a total lack of Hassall's bodies. The rate of decreased thymic function in tumor development is discussed. (31 references)

- 1272 THE ROLE OF THE THYMUS IN CARCINOGENESIS. (Rus.) Andrianova, M. M. (Inst. Nutr. Acad. Med. Sci., Moscow, U.S.S.R.). *Vop Onkol* 16(12):94-103, 1970.

The immunological implication of the thymus in the development of neoplasia is reviewed. The function of the thymus may be defined by 3 hypothetical mechanisms: 1) as a primary source of lymphocytes; 2) as an immune response generator by which the lymphocytes passing through the thymus become immune competent; 3) as a producer of a humoral factor effective in the development of the lymphatic system of the growing organism. Reference is made to the disruption of immune response by thymectomy of newborn animals which affects the synthesis of globulins and the capabilities of antibody formation. Thus viral carcinogenesis induced by polyoma virus, SV40 or some of the adenoviruses is enhanced in newborn thymectomized mice, rats, rabbits or hamsters. The enhancement by thymectomy of chemical carcinogenesis by 3,4-benzpyrene, 3-methylcholanthrene or

7,12-dimethylbenz(a)anthracene seems to be less evident. Thymectomy of the adult animal which has an established lymphatic system affects its immune defense mechanisms to a lesser extent. Lymphoid leukosis (Gross virus) constitutes a special case in terms of thymus involvement, in that the thymus seems to be necessary for its development. The mechanisms involved in the thymus-controlled immunological functions are still not well defined. (148 references)

- 1273 COMPARATIVE ONCOLOGY AND ENVIRONMENTAL CARCINOGENS. (E.) Dawe, C. J. (Bethesda Md.). *UICC Bull Cancer* 8(4):2-3, 1970.

Studies presently underway to investigate the development of neoplasms by aquatic animals and to elucidate possible etiological factors are reviewed. Bottom-feeding fish and filter-feeding mollusks provide test systems for investigating tumorigenesis by chemical water contaminants. Filter-feeders which accumulate many chemical contaminants in high concentrations in the course of ingesting food and the bottom-feeders which subsist on these mollusks demonstrate the carcinogenic properties of water contaminants. Epitheliomas developing in the mantles of the Sydney rock oyster are under study as are carcinomas and papillomas developed by California coastal croakers. Eel papillomas and papillomas of fish such as the founder and the sole are thought to be of viral origin. Neuroepitheliomas developed by Lake Michigan whitefish are also of interest in view of the extreme pollution of the Great Lakes. Lymphosarcomas developed by the northern pike, which is neither a bottom-feeder nor a scavenger, are also being studied. (no references)

- 1274 COMPARATIVE METABOLISM OF RADIONUCLIDES IN MAMMALS: A REVIEW. (E.) Stara, J. F. (Natl. Ctr. Radiol. Hlth., Cincinnati, O.), Nelson, R. J. Della Rosa and L. K. Bustad. *Health Phys* 20(2):113-137, 1971.

Animal and human metabolism studies for selected hazardous radionuclides are reviewed. Iodine-131 and the strontium isotopes have been shown to produce particularly deleterious effects when ingested. Iodine-131 produces most of its effects in the thyroid region due to localized deposition, with changes occurring more rapidly in rodents than in dog or man as well as the fetus in both animal and man. Alkaline earths and plutonium are deposited primarily in skeletal tissue and show their effects in osseous tissue and the blood-forming tissues; single dose effects include osteosarcomas and chronic exposure results in myelogenous leukemia, lymphosarcoma and reticulum cell sarcoma in animals and man. Beagles which are fed high levels of radioactive strontium develop myeloproliferative disorders resembling granulocytic leukemia in the acute form and myelofibrosis with myeloid metaplasia in the chronic form with the earliest onset occurring at 14 months-of-age with cumulative radiation doses of at least 100 rads and with an age-dose relationship in incidence. Similarities in the metabolism of radioisotopes in

many mammalian species permits a cautious extrapolation to man only when utilizing several species from different sub-families with life spans of different duration. (201 references)

- 1275 DRUGS, FOOD ADDITIVES, AND PESTICIDES IN RELATION TO ENVIRONMENTAL CANCER IN MAN: HISTORICAL PERSPECTIVES. (E.) Friedman, L. (Food Drug Admin., Washington, D. C.). *FDA By-Lines* 1(4): 179-184, 1971.

Accepted testing procedures for assessing the carcinogenicity of food additives, pesticides and other drugs in the human population were briefly reviewed. Demonstration of carcinogenicity for a given chemical is complicated by the fact that not all members of a population exposed to that drug will develop cancer; in addition, long periods of exposure are required for even potent carcinogens to produce cancer in humans. Moreover, laboratory findings do not necessarily predict the reaction of humans to the test agent (however, known human carcinogens generally elicit cancer in laboratory animals). A major task for research is to identify not the potent carcinogens whose effects are conspicuous but the weak carcinogens which are more likely to be overlooked. Chronic toxicity tests prolonged for the lifetime of the test animals are valuable for identifying agents potentially dangerous for man. Increasing concern that food additives and pesticides may have carcinogenic efficacy for men has created a need to know the carcinogenic potential of every food component. Test systems used to fill this need must employ several animal species, positive controls using chemicals similar to the test compound, and a variety of dosages. Drugs should be administered by routes analogous to the routes by which humans ingest them. A toxic response in the laboratory will show only that the agent is putatively carcinogenic for humans; a negative result, however, cannot exclude the possibility that the test substance is carcinogenic for man. Rapid test models for carcinogenicity should be developed in order to shorten the protracted lengths of time involved in lifetime evaluations of chemical carcinogens. (10 references).

- 1276 MYCOTOXINS AND THEIR ROLE IN ONCOGENESIS, WITH SPECIAL REFERENCE TO BLOOD DISEASES. (E.) Aleksandrowicz, J. (no affil), M. Czachor, A. Schiffer and B. Smyk. *Haemat Latina* 8(2):115-124, 1970.

The role of fungal metabolites (specifically mycotoxins) in carcinogenesis was investigated in a review of the literature. Two groups of diseases caused by mycotoxins were discussed: syndromes characterized by aplasia of the bone marrow such as erythro-, thrombo- and granulocytopenia; and syndromes resembling parenchymatous hepatitis or neoplastic proliferation of liver cells. Syndromes in the first group resemble acute leukemia in its early stages; fungi producing myelotropic mycotoxins include fungi of the *Fusarium* group. These mycotoxins which are steroids are often ingested via poorly stored grains on which the fungi grow.

The best known hepatotropic mycotoxin is aflatoxin, a metabolite of the fungus *Aspergillus flavus*. The cultivation of groundnuts in some parts of Africa and the consumption of moldy food products in other parts of the world have been implicated in carcinogenesis by means of aflatoxins. (24 references)

- 1277 A REVIEW OF OCCUPATIONAL CANCER. (E.) Emara, A. M. (Fac. Med. Cairo U., Egypt). *J Egypt Med Ass* 53(6):496-510, 1970.

The literature documenting the development of cancer in various sites resulting from occupational exposure to various carcinogenic agents is reviewed. The site of malignant development most heavily implicated in occupational carcinogenesis is the skin. Among carcinogenic agents thought to be responsible for the production of skin cancer are chimney soot (scrotal carcinoma), paraffin, oils and petroleum products, arsenic, and charcoal smoke. Lung cancer ranks second to skin cancer among the occupational cancers and has been reported in connection with nickel refining, chromate manufacture, asbestos exposure, coal tar exposure, arsenic exposure incurred in the course of sheep-dipping operations, iron mining, isopropyl oil manufacture, beryllium working, and wood working. Bladder cancer has been observed to have high incidences in workers with aniline dyes; xenylamine exposure has also been implicated. Ionizing radiation has been connected with leukemia, as has chronic benzol poisoning. Oil-soluble azo-dyes have been linked to liver tumors, and workers with arsenical sprays frequently develop liver tumors. Painting of luminous dials on watches has been connected with the development of osteogenic sarcomas. (142 references)

- 1278 CANCER GENETICS. (E.) Lynch, H. T. (Creighton U. Sch. Med., Omaha, Nebraska) and A. J. Krush. *South Med J* 64(suppl. 1):26-40, 1971.

The clinical properties and pathology of congenital malignant diseases were reviewed. Familial polyposis coli, inherited as a simple dominant, progresses to adenocarcinoma in about 40% of cases and can be expected to affect about 50% of the relatives of any patient. Gardner's syndrome (soft tissue and bony tumors and adenomatous polyps of the colon) has been observed in a series of 4 families of which 315 members were examined; of these 315, 73 exhibited symptoms of Gardner's syndrome, and 26 developed adenocarcinomas. Von Recklinghausen's disease (neurofibromatosis), is inherited as an autosomal dominant; patients develop sarcomas in 8-20% of cases, as well as cutaneous lesions, acoustic neuromas, and pheochromocytomas. Xeroderma pigmentosum, inherited as an autosomal recessive, may involve a variety of neurologic, endocrinologic and skeletal manifestations as well as skin lesions. Affected patients have a heightened sensitivity to solar radiation. The frequency of melanoma, inherited as an autosomal dominant is unknown, but has been estimated at about 3%. In 1 family, 3 of 14 members in 4 generations were affected. Other inherited malignancies include endometrial carcinoma and multiple nevoid basal cell

carcinoma. In the former condition, 1 study has shown that endometrial carcinoma occurred in 16% of first degree relatives in 154 cases. Cancer of the colon, including Peutz-Jeghers syndrome, Turcot's syndrome, solitary colon polyps, ulcerative colitis, and juvenile polyposis coli, are other conditions having familial occurrence. Hereditary factors may operate in some cases of mammary carcinoma. Approximately 50% of the neoplasms present at birth were neuroblastomas and 50% were sarcomas in one study. Other childhood conditions thought to be congenital include Wilms' tumor. (73 references)

- 1279 FAMILIAL ENDOCRINE ADENOMATOSIS: REPORT OF ONE CASE AND REVIEW OF THE LITERATURE. (Fr.) Croisier, J. C. (Hosp. Pitie, Paris, France), E. Azerad and J. Lubetzki. *Sem Hop Paris* 47(8):494-525, 1971.

The details of the reported case of familial endocrine adenomatosis included evidence of primary hyperparathyroidism, pancreatic islet cell damage (beta, alpha₁ and alpha₂), a thyroid nodule, nodular bilateral adrenocortical hyperplasia, and an increase in blood histamine and serotonin. The 2 dominant complaints on admission were hypoglycemic accidents and epigastric pain. A surgical intervention was necessary when the epigastric pain became violent; a perforated duodenal ulcer and 2 pancreatic tumors were revealed, at which time a gastro-duodenectomy was performed. Post-operative treatment is described. In general, the disease is familial and hereditary; it is transmitted genetically as an autosomic dominant, and characterized by proliferation foci in at least 2 endocrine glands. The most frequently affected glands are the parathyroid (88%), pancreas (84%), pituitary (51%), the adrenal cortex (41%) and the thyroid (27%). (249 references)

- 1280 CHRONIC MYELOID LEUKEMIA AND CHROMOSOMES. (Fr.) Berger, R. (Hosp. Child. Dis., Paris, France). *Rev Europ Etud Clin Biol* 15(9):1000-1007, 1970.

Cytogenetic studies of chronic myeloid leukemia have shown that the Philadelphia (Ph) chromosome is not the only karyotype anomaly in this disease. The Ph chromosome may characterize the acute stage of the disease whereas various other anomalies appear additionally in the chronic stage. Cases taken from the literature, having the Ph chromosome in common, were categorized into 5 groups of anomalies: the first, a loss of the G or Y chromosome; the second, an excess of C chromosomes and a rapid duplication of Ph, or an excess of D chromosomes coincident with Ph duplication; the third, an acquisition of F and C chromosomes accompanying the Ph duplication; the fourth, a loss in the E chromosomes and an increase in C chromosomes; and the fifth, anomalies different from the other groups, such as an excess in chromosome 16 or abnormalities in the A and B groups. Attention is drawn to the rarity of some of the combinations of anomalies, as in the case of the A and B groups and in E and F. The coexistence in the same

cell of an excess of F and a loss of chromosome 17-18 is quite exceptional. The possible interpretatic of such patterns of chromosome anomalies are discussed. (55 references)

- 1281 THE PROLIFERATIVE KINETICS OF THE ACUTE LEUKAEMIAS IN RELATION TO THEIR TREATMENT. (E.) Gavosto, F. (Gen. Med. Clin., U. Turin, Italy). *Rev Eur Etud Clin Biol* 15(10):1042-1047, 1970.

The growth pattern of human leukemias indicates that a proportion of the leukemic cell population is non-dividing. The pool of proliferating cells in acute human leukemias appears not to be self-maintaining; since dividing cells often produce cells which do not themselves proliferate, the cell birth rate in the proliferating portions of tumor cells is not exponential. Recent findings of human leukemia cells in the Go phase where cells are outside the cell cycle but are able to reenter it (under normal conditions or after treatment with chemical agents) suggest that cells in the Go phase play an important role in determining the growth kinetics of human leukemias. Part of the stem cell population responsible for tumor growth may be in the Go phase; at any time, a fraction of these Go cells may become activated to feed the proliferation cell pool of the tumor, while other Go cells remain outside the cell cycle in the non-proliferating pool and still other cells have returned to the Go phase after a period in proliferation. The possible value of agents which affect the number and/or behavior of cells in the Go phase and therefore the growth pattern of leukemia are discussed in terms of chemotherapy. (20 references)

- 1282 HYPERPLASIA AND CARCINOMA OF THE ENDOMETRIUM. (E.) Bettinger, H. F. (Roy. Women's Hosp., Melbourne, Australia). *Amer J Obstet Gynec* 109(2):194-197, 1971.

Advances in the understanding of the development of endometrial carcinoma from hyperplasia of the corpus uteri were reviewed. Since 1900, the association of hyperplasia and carcinoma has been observed and it has been suspected that the former condition is an early stage in the development of uterine or endometrial cancer. Stages of hyperplasia have been described, including "ordinary" hyperplasia and "atypical" hyperplasia; however, the factors determining the transition from one stage to the other remain unclear. Stimulation of the mucosa by estrogens, and hormonal imbalance have both been implicated in the genesis of hyperplasia and with its transition to "carcinoma in situ." The evidence is that the development of endometrial carcinoma is often preceded by many years by atypical hyperplasia glandular hyperplasia may not become malignant, but atypical hyperplasia, if not checked, will usually develop into carcinoma. It has been shown that hyperplasia may react well to treatment with progesterone; such treatment blocked development of carcinoma in one study. Although the evidence indicates that carcinoma of the endometrium is preceded by hyperplasia, it has also been shown that carcino

a may develop from endometrial cells in intermediate stages of hyperplastic development; carcinoma *in situ* and atypical hyperplasia are stages which may be bypassed. Opportunities for investigating the relationship between hyperplasia and carcinoma are being reduced by the practice of performing hysterectomies on many patients with early hyperplasia. (15 references)

1283 MELANINS AND CARCINOGENESIS. (Pol.)
 Pytniewski, Z. (Acad. Med. Gdansk, Poland). *Pol
 yg Lek* 26(3):110-112, 1971. (28 references)

1284 TUMORS AND BLOOD GROUPS. (It.) Gualandri,
 V (Inst. Tumor Genet., U. Milan, Italy). *Tumori*
 56(4):199-206, 1970. (15 references)

1285 SYMPOSIUM ON NATURALLY OCCURRING CARCINO-
 GENS; PRAGUE, APRIL 14-15, 1970. (Ger.)
 Schramm, T. (Inst. Cancer Res., Berlin, Germany) and
 W. Gibel. *Arch Geschwulstforsch* 36(3):282-284, 1970.
 (No references)

1286 MALIGNANT TUMORS AND MICROORGANISMS. (Ger.)
 Gericke, D. (Hoechst Dye Plants, Frankfurt/
 M, Germany) *Fortschr Med* 89(1):32-35, 1971. (35 references)

- 1287 THE ONCOGENICITY OF TWO 1,1-DIARYL-2-PROPYNYL N-CYCLOALKYL CARBAMATES. (E.) Harris, P. N. (Eli Lilly Co., Greenfield, Ind.), W. R. Gibson and R. D. Dillard. *Cancer Res* 30(12):2952-2954, 1970.

The carcinogenicity of 1,1-bis(4-fluorophenyl)-2-propynyl N-cyclooctylcarbamate and 1,1-bis(4-fluorophenyl)-2-propynyl N-cycloheptylcarbamate was investigated in rats. Rats were maintained on a 3 month dietary regimen of the compounds in concentrations of 0.05, 0.1, or 0.25% (the cyclooctyl compound) and 0.01, 0.025 or 0.05% (the cycloheptyl derivative). Eighteen of 25 rats given the cyclooctyl compound developed malignant lymphoma; 2 developed malignant lymphoma and colonic adenocarcinoma, and 2 developed ileal adenocarcinoma. In these rats, the latency period for tumor development was 55 days. Nineteen of 37 rats given the cycloheptyl derivative developed malignant lymphoma and mammary adenocarcinoma; 2 developed mammary adenocarcinoma alone. The latency for tumors in the cycloheptyl derivative was 54 days.

- 1288 ALTERATIONS IN CREATINE KINASE ACTIVITIES DURING HEPATOCARCINOGENESIS. (Rus.) Ostretsova, I. B. (N. N. Petrov Sci. Res. Inst. Oncol. Leningrad, U.S.S.R.). *Vop Onkol* 16(11):102-104, 1970.

Mouse liver creatine kinase activity following s.c. administration of 0.04 ml carbon tetrachloride (single dose) increased by 30-40% in 2 days and 300% by 4 days after the injection. A gradual decrease in creatine kinase which reached normal values on the 3rd wk after the administration of the hepatotropic carcinogen was followed by a slight increase towards the end of the experimental period of 41 days. Similar trends in creatine kinase activity were noticed in transplanted 22a hepatomas in C3HA mice. The variations in carbon tetrachloride-treated mouse liver creatine kinase activities appear to be related to a carcinogenic rather than to a toxic action of carbon tetrachloride. The increase in creatine kinase activity in both hepatoma and liver tissue exposed to carbon tetrachloride may be related to an epigenetic unblocking of the protein synthesis determining genes.

- 1289 INVESTIGATIONS ON POSSIBLE CARCINOGENIC EFFECTS OF β -SEVIN. (Rus.) Zabezhinskiy, M. A. (N. N. Petrov Sci. Res. Inst. Oncol. Leningrad, U.S.S.R.). *Vop Onkol* 16(11):106-107, 1970.

Carcinogenicity of β -sevin, (2-naphthyl N-methylcarbamate), was tested in randombred white rats and CC57W mice. β -Sevin was given to 100 rats (50 mg s.c. once a wk for 33 months) and to 50 mice (20 mg once a wk for 24 months); 50 rats and 50 mice were treated p.o. daily with 25 mg and 10 mg. resp., 5 times a wk for 33 and 24 months, resp. S.C. administration of β -sevin produced fibrosarcoma at the injection site in 2 rats and s.c. rhabdomyosarcoma in 5 of the 29 surviving rats 21-30 months after the beginning of the experiment. Oral treatment induced a liver sarcoma and a fibroadenoma of the mammary gland in 1 rat, adenocarcinoma of the mammary gland in 3 rats, malignant thymoma in 1 rat and an ovarian

tumor in 1 of the 16 surviving rats 23-35 months after the beginning of the experiment. S.C. treatment with β -sevin induced lung adenoma in 4 mice, liver adenoma in 1 mouse, mediastinal hemangioma in 1 mouse and leukosis in 2 of the 10 surviving mice 15-20 months after the treatment. Oral treatment produced leukosis in 2 mice in 13-15 months, lung cancer in 2 mice in 15-16 months and liver hemangioma in 4 of the 26 surviving mice 15-23 months after the beginning of the experiment. The incidence of tumors in rats was 25% following both routes of administration. None of the control rats developed tumors. Tumor incidence in mice was 60% after s.c. treatment and 31% following p.o. treatment. However, some of the control mice also developed tumors. Carcinogenic activity appears to depend on the presence of the carbamyl moiety in the β -position of the naphthyl group, since α -sevin is noncarcinogenic.

- 1290 CARCINOGENICITY OF THE PESTICIDES SEVIN, MANEB, CIRAM AND CINEB. (Rus.) Andrianova, M. M. (Acad. Med. Moscow, U.S.S.R.) and I. V. Alekseeva. *Vop Pitani* 29(6):71-74, 1970.

The carcinogenicity of sevin, maneb, ciram and cineb was tested by p.o. and s.c. administration to randombred rats. Each pesticide was given p.o. as a suspension in water (30 mg/kg sevin, 335 mg/kg maneb, 70 mg/kg ciram or 285 mg/kg cineb) twice a wk for 22 months to experimental groups of 60 rats each. S.C. treatment consisted in a hip implant of paraffin pills containing 20 mg sevin, 12.5 mg maneb, 15 mg ciram or 20 mg cineb to 4 groups of 48 rats each. Tumors were noticed 22 months after the beginning of the experiment in all of the experimental groups. Sevin (p.o.) induced tumors in 4 of 10 rats (2 fibrosarcomas of the right hip, 1 polymorphous cell sarcoma of the mediastinum and 1 osteosarcoma); s.c. treatment resulted in fibrosarcomas in 2 of 10 rats. Maneb treatment (p.o.) induced tumors in 2 of 10 rats (1 mammary gland carcinoma and 1 rhabdomyosarcoma of the left hip), and s.c. treatment resulted in 1 carcinoma of the thyroid, 1 fibrosarcoma in the neck region and 1 sarcoma of the mediastinum in 3 of 4 rats. Ciram administration (p.o.) produced tumors in 4 of 10 rats (2 malignant hepatomas, 1 subcutaneous fibrosarcoma and 1 subcutaneous polymorphous cell sarcoma in the spinal and neck region, resp. when applied s.c., tumors occurred in 3 of 10 rats (1 hepatoma, 1 lymphosarcoma of the colon and 1 s.c. fibrosarcoma in the hip region). Cineb given p.o. produced tumors in 2 of 10 rats (1 adenocarcinoma of the colon and 1 intestinal lymphosarcoma), and with s.c. treatment 4 of 10 rats developed tumors (1 hepatoma, 1 fibrosarcoma of the gastric wall, 1 subcutaneous rhabdomyosarcoma of the hip and 1 spindle cell sarcoma of the right anterior limb). Of the 48 control animals 1 of 46 developed fibrosarcoma 11 months after the beginning of the experiment. No tumor development occurred at the site of implantation of the pesticides indicating that these pesticides exhibit a general carcinogenic action in rats.

- 1291 CARCINOGENICITY OF ISOSTERS OF EPOXIDES AND LACTONES: AZIRIDINE ETHANOL, PROPANE SULFONE, AND RELATED COMPOUNDS. (E.) Van Duuren,

B. L. (New York U. Med. Ctr., New York, N. Y.), S. Melchionne, R. Blair, B. M. Goldschmidt and C. Katz. *J Nat Cancer Inst* 46(1):143-149, 1971.

The carcinogenicity of low molecular wt compounds including epoxides, their nitrogen or sulfur analogs, a polymeric aldehyde, and an acetal were investigated in mice. Mice were maintained on a lifetime (63-93 wk) regimen of s.c. injections of the test agents. Propane sultone (1-propanesulfonic acid-3-hydroxy- γ -sultone) and aziridine ethanol (β -hydroxy-1-ethyl-aziridine) induced sarcomas at the injection site when administered in doses of 0.3 mg/0.05 ml distilled water. Twenty-one of 30 mice injected with propane sultone developed 12 sarcomas, 1 carcinoma, 7 adenocanthomas and 1 papilloma. Ten of 30 mice given aziridine ethanol developed sarcomas. The compounds 3,4-epoxysulfolane, 1,2-epoxybutyronitrile, 3,4-dihydroxy-3-cyclobutene-1,2-dione, ethyl-2,3-epoxybutyrate, tetramethyl-1,3-cyclobutanedione, perchloro-2-cyclobutene-1-one, and polymeric dialdehyde induced less than 3 tumors at the sites of their injections. The following compounds failed to induce tumors: 3-sulfolene, 3,4-epoxybutanal diethylacetal, 5,6-epoxyhexanal diethylacetal, and N,N-dimethylformamide dimethylacetal.

1292 AVIDITY OF FOLIC ACID FOR CARCINOGENIC METAL IONS, ALUMINIUM(III), CHROMIUM(III), BERYLLIUM(II), LEAD(II) AND URANIUM(VI). (E.) Nayan, R. (Chem. Lab., U. Allahabad, India) and A. K. Dey. *Z Naturforsch* 256(12):1453-1457, 1970.

The chelate formation of folic acid with the carcinogenic metal ions, aluminum (III), chromium (III), beryllium (II), lead (II) and uranium (VI) has been studied with the Bjerrum-Calvin pH-titration technique. Chelates at biological pH were formed only with the phenolic form of folic acid; no sharp change was seen in the shape of the chelate-formation curves at different ionic strengths, suggesting that the various species coexist in solution.

1293 DEVELOPMENT OF HEPATIC TUMORS IN RATS FOLLOWING INGESTION OF *SENECIO LONGILOBUS*. (E.) Harris, P. N. (Eli Lilly Co., Greenfield, Ind.) and K. K. Chen. *Cancer Res* 30(12):2881-2886, 1970.

The effects of prolonged administration of dried *Senecio longilobus* (SL) in the diet of rats on the development of hepatic tumors and associated manifestations is reported. In rats receiving a continuous diet of 0.75% SL, deaths began to occur rapidly after 1 month with longest survival time being 131 days; at 0.5% concentrations survival times increased somewhat with 4 rats living more than 200 days. Of 31 rats receiving 0.5% concentrations for 1 month followed by a 2-wk SL-free diet for a period of 1 yr and of those given 0.5% Senecio diet for 1 wk alternated with 1 wk SL-free diet for 1 yr, 22 survived from 419-657 days. Rats with a survival time of less than 3 months demonstrated pulmonary edema sometimes associated with hydrothorax or ascites, pneumonia, pulmonary congestion and intra-alveolar hemorrhage, and epithelial proliferation only occasionally. With

increasing age, the number and foci of proliferation increased to 7% for the entire group and was 31% for survivors after 300 days. Incidence of pulmonary arteritis was 50% in rats dying before 100 days, 20% between 100 and 300 days, and 6% in those dying after 300 days, with thrombosis of small vessels occurring commonly. Albumin/globulin ratios determined in 9 rats were reversed and liver cell necrosis was observed in nearly 20% of the rats that died during the first 3 months; after short exposure to SL, some livers were dark, reddish-brown, friable and of normal size. Later they diminished in size and demonstrated hypertrophic parenchymal cells and nuclei with regeneration leading to formation of nodules suggestive of neoplasm greater than 1 cm diameter and bile duct proliferation with formation of cholangiocystomas. After 428 to 657 days, four had hepatocarcinomas with central necrosis proliferating to portal veins and branches of the pulmonary arteries.

1294 THE EFFECT OF CHRONIC ESTROGENIC STIMULATION ON THE SQUIRREL MONKEY CERVICAL EPITHELIUM. (E.) Graham, C. E. (Yerkes Reg. Primate Res. Ctr., Emory U., Atlanta, Ga.) and S. L. Manocha. *Virchow Arch Zellpath* 7(2-3):147-156, 1971.

Estradiol benzoate implantation in squirrel monkeys was used to study epidermization of the cervical epithelium in response to chronic estrogenic stimulation. Stratified squamous epithelium of the vagina and cervix became clearly demarcated from columnar epithelium with no essential difference noted in response to 10% or 95% estradiol benzoate pellets. Stimulation with pellets of 100% diethylstilbestrol for periods of 5 or more months resulted in isolated foci of varying size of partially cornified stratified epithelium compared to control animals which demonstrated only occasional small islands of apparently isolated stratified cells. No areas of epithelium could be recognized as intermediate in morphology between normal columnar and normal stratified epithelium. Glycogen content was most prominent in the intermediate layer of the cervical stratified epithelium and became depleted after treatment with diethylstilbestrol, whereas in controls this glycogen content increased. The activity of phosphorylases, alcohol dehydrogenases and simple esterases was enhanced in the experimental animals, while 6-phosphogluconate dehydrogenase and ATPase were somewhat reduced; no apparent changes in alkaline or acid phosphatase reactions were observed in either experimental or control animals. New squamous cells appeared to be an outgrowth from the stratified squamous epithelium at the squamocolumnar junction, rather than from squamous metaplasia of columnar cells.

1295 THE SYNERGISM BETWEEN RADIATION AND ESTROGEN IN THE PRODUCTION OF MAMMARY CANCER IN THE RAT. (E.) Segaloff, A. (Alton Ochsner Med. Found., New Orleans, La.) and W. S. Maxfield. *Cancer Res* 31(2):166-168, 1971.

Rats implanted with pellets containing estrogen (25% diethylstilbesterol, 75% cholesterol) and ir-

radiated with 800 r to the center of the mammary chain developed more mammary carcinomas after a shorter latency than rats given estrogen alone, or irradiation alone. Twelve of 14 rats given estrogen and radiation developed a total of 78 palpable mammary tumors on the irradiated mammary chain; the first tumor appeared 18 wk after irradiation. The mammary chain which was shielded from radiation in estrogen-treated rats developed a total of 17 tumors after 29 wk latency. Rats which were given estrogen pellets only, without irradiation, developed mammary tumors in 15/16 cases; the total number of tumors developed by this group was 54, and the latency was 20 wk. Rats given radiation alone, without estrogen, developed tumors in 8/11 cases; the total number of tumors developed by this group was 12 and the latency was 75 wk. Apparently, a synergism exists between the actions of X-irradiation and estrogen treatment in the rat mammary carcinogenesis.

- 1296 ULTRASTRUCTURAL ALTERATIONS WITHIN HYPERPLASTIC LIVER NODULES INDUCED BY ETHIONINE. (E.) Merkow, L. P. (W. H. Singer Mem. Res. Inst., Allegheny Gen. Hosp., Pittsburgh, Pa.), S. M. Epstein, M. Slifkin, E. Farber and M. Pardo. *Cancer Res* 31(2):174-178, 1971.

The effect of ethionine-induced liver hyperplasia on cellular ultrastructure was studied in male Wistar rats by electron microscopy. Examination of cells from fasted animals with ethionine-induced nodules showed a marked clustering and aggregation of the smooth endoplasmic reticulum with corresponding diminution in rough endoplasmic reticulum which was closely apposed to the mitochondria. In addition, multivesicular bodies in close proximity to both the Golgi complex and the clusters of smooth endoplasmic reticulum were observed; these changes were remarkably similar both within any one nodule and from one hyperplastic liver nodule to another. Nonnodular liver adjacent to hyperplastic liver nodules showed a remarkable preservation of subcellular organelles and organization in both fed and fasted animals. Nodular cells obtained from fed rats maintained both normal intra- and intercellular relationships. The cytostructural alterations appear to represent a specific set of subcellular reaction patterns confined to the hyperplastic liver nodule, which differs markedly from that noted in hepatocellular carcinoma cells.

- 1297 MITOTIC, CHROMOSOMAL, AND NUCLEOLAR ALTERATIONS INDUCED BY THIOACETAMIDE IN RELATION TO THE MITOTIC CYCLE AFTER PARTIAL HEPATECTOMY. (E.) Mironescu, S. (Inst. Endocr., Bucharest, Rumania) and M. Ciovirnache. *J Nat Cancer Inst* 46(1):49-61, 1971.

Induction of mitotic, chromosomal and nucleolar alterations within the mitotic cycle by thioacetamide (150 mg/kg) after partial hepatectomy was studied in male Wistar rats by means of tritiated thymidine. Almost all hepatocytes proliferated after partial hepatectomy at a 90-95% level, with 8% labeling in DNA synthesis during the 22nd hr followed by a steady flux of cells through synthe-

sis at a rate of 3-4% per hour. Thioacetamide did not increase the number of cells entering DNA synthesis nor did it raise the low incidence of abnormal nucleoli during the first 12 hr. When given at later intervals, increased numbers of nuclei with "aniso" nucleoli were induced and reached a peak value when the carcinogen was given 18 hr after partial liver removal. The earliest detectable alteration induced by the carcinogen was nucleolar hypertrophy, and Colcemid and vinblastine effectively blocked most cells entering mitosis 25-31 hr after partial hepatectomy at metaphase. The apparent S-phase dependence of thioacetamide chromosomal aberrations suggests that the damaging action is exercised on cells already in S and although morphologically similar to those induced by other agents, the mechanism of action is not identified.

- 1298 THE BINDING OF N-HYDROXY-2-ACETYLAMINO-FLUORENE TO REPLICATING AND NONREPLICATING DNA IN RAT LIVER. (E.) Jackson, C. D. (U. Tennessee Med. Unit, Memphis) and C. C. Irving. *Chem Biol Interact* 2(3):261-265, 1970.

Male rats were given i.p. injections of ^{14}C -labeled N-hydroxy-2-acetylaminofluorene and 250 μC of tritiated 5-bromo-2'-deoxyuridine in order to determine whether the former compound was bound to rat liver DNA which is replicating or to nonreplicating DNA. Newly replicated DNA, which had incorporated ^3H -5-bromo-2'-deoxyuridine, was found to band on CsCl density gradients at an average density greater than that of the bulk of the DNA. The distribution of the carcinogen N-hydroxy-2-acetylaminofluorene which was bound to DNA *in vivo* was coincident with the distribution of the bulk of the DNA, indicating that this carcinogen did not bind to DNA exclusively during replication.

- 1299 REGRESSION AND PERSISTENCE OF HYPERPLASTIC HEPATIC NODULES INDUCED BY N-2-FLUORENYL-ACETAMIDE AND THEIR RELATIONSHIP TO HEPATOCARCINOMAS. (E.) Teebor, G. W. (New York U. Sch. Med., New York, N. Y.) and F. F. Becker. *Cancer Res* 31(1):1-1971.

The development of hyperplastic nodules and hepatic carcinomas in the livers of rats fed N-2-fluorenyl-acetamide (2-FAA) was investigated in the belief that the nodules represent an early stage of malignant change. Male rats were given a diet containing 0.02% 2-FAA for three 3-wk periods; another group of rats was given the 2-FAA diet for four 3-wk periods. At the end of the 3 cycle feeding period, 45 of 50 rats had developed nodules on the surface of the liver; 2 months after cessation of 2-FAA feeding, 12 of 25 rats showed nodules, and by 6 months after 2-FAA feeding, only 2 of 25 rats had nodules. Only 1 of 25 rats fed with 2-FAA in the 3-cycle feeding regimen developed hepatocellular carcinoma. At the end of 4-cycle feeding regimen, 75 of 80 rats had developed nodules; at 6 months after the cessation of the 4-cycle feeding regimen, 26 of 37 rats showed nodules, and 12 months 14 of 23 rats had developed hepatomas.

which never developed nodules, and rats in which nodules regressed completely, never developed hepatomas. The results appeared to suggest that a linear relationship exists between the hyperplastic nodule and hepatocellular carcinoma development.

- 1300 DISORGANIZATION OF MOUSE BLADDER EPITHELIUM INDUCED BY 2-ACETYLAMINOFLUORENE AND 4-ETHYLSULFONYLNAPHTHALENE-1-SULFONAMIDE. (E.) Levi, P. E. (Dept. Exp. Path. Cancer Res., Leeds, England), J. C. Knowles, D. M. Cowen, M. Wood and E. H. Cooper. *J Nat Cancer Inst* 46(2):337-352, 1971.

Modification of the bladder epithelium of female A x IF mice fed 4-ethylsulfonylnaphthalene-1-sulfonamide (ENS) or 2-acetylaminofluorene (AAF) was studied by the use of electron and light microscopy. Bladder epithelium of mice fed AAF for 4-12 wk showed an increase of 3 to 5 cell layers with mitotic activity, DNA measurements of nuclei and distribution of alkaline phosphatase were similar to that in the controls. Two main types of modification of the ultrastructure that were observed in these cells were that the cytoplasm of the large surface cells had few fusiform vesicles, and the lysosomes were often surrounded by a series of concentric, double membranes. After 20 wk, the membrane whorls regressed, the mitochondria were abnormal, and the unit membrane of the surface cells was asymmetric. The response to ENS after 4 wk was crystalluria, and after 8 wk large concretions of calcium phosphate and oxalate were present in the bladder. Pronounced hyperplasia 6-8 cell layers thick occurred with the percentage of cells in mitosis varying considerably from one animal to another, ranging from the normal 0.01% to about 10%, and marked inflammatory changes in connective tissue with edema and extensive infiltration of polymorphonuclear leukocytes and lymphocytes occurred. Dedifferentiation and a loss of alkaline phosphatase activity occurred after 8 wk, while the ultrastructure showed a striking loss of characteristic organelles with formation of dark, osmiophilic inclusions which eventually destroyed the mitochondria. Return to a normal diet for 8 wk resulted in loss of crystalluria and a virtually normal histological appearance and normal alkaline phosphatase distribution.

- 1301 DIFFERENCES IN THE BINDING OF 2-ACETYLAMINOFLUORENE AND ITS N-HYDROXY METABOLITE TO LIVER NUCLEIC ACIDS OF MALE AND FEMALE RATS. (E.) Irving, C. C. (VA Hosp., U. Tennessee, Memphis) and R. A. Veazey. *Cancer Res* 31(1):19-22, 1971.

Covalent binding of the carcinogens 2-acetylaminofluorene (AAF) and N-hydroxy-acetylaminofluorene (N-hydroxy-AAF) to liver nucleic acids of male and female rats was investigated in order to explain the observation that male rats are more prone to induction of liver cancer by these compounds than are female rats. Rats were given s.c. injections of ¹⁴C-9-labeled AAF or N-hydroxy-AAF in amounts of 30 mg/kg body wt 16 hr before sacrifice, and tRNA, rRNA and DNA were isolated in liver preparations. Livers of male rats given AAF were able to bind

123 picomoles of the compound/mg tRNA and 42-44 picomoles/mg rRNA. Females were able to bind 71 picomoles AAF/mg tRNA and 26-29 picomoles/mg rRNA. When N-hydroxy-AAF was injected, the amounts which were bound to nucleic acids were 160 picomoles/mg tRNA for males and 55 picomoles/mg rRNA for females. No sex differences were found in the binding of total radioactivity to liver DNA after injection of either compound, and amounts of compound able to bind to DNA did not differ by more than 3 picomoles between males and females. Seventy-two percent of the fluorene residues which were bound to rRNA, and 37% of those which were bound to DNA retained the N-acetyl group in males, while in females 33% of the fluorene residues which were bound to rRNA and only 7% of those which were bound to DNA retained the N-acetyl group. The mechanisms of N-hydroxy-AAF metabolic activation as well as the amounts of AAF which bind to liver nucleic acids seemed to show sex differences in rats.

- 1302 STUDIES OF EXPERIMENTAL BLADDER CARCINOMA IN FISCHER 344 FEMALE RATS: I. INDUCTION OF TUMORS WITH DIET LOW IN VITAMIN B₆ CONTAINING N-2-FLUORENYLACETAMIDE AFTER SINGLE DOSE OF CYCLOPHOSPHAMIDE. (E) Koss, L. G. (Sinai Hosp. Baltimore, Md.) and P. Lavin. *J Nat Cancer Inst* 46(3):585-595, 1971.

All 17 rats in a group given 100-200 mg/kg cyclophosphamide and placed on a diet deficient in pyridoxine and containing 600 mg/kg N-2-fluorenylacetamide (FAA) developed carcinoma of the urinary bladder; in 16 cases, the tumors were invasive. Carcinomas appeared beginning 6.75 months after initiation of the carcinogenic diet. Three of 5 rats given the carcinogenic diet without cyclophosphamide developed carcinoma of the bladder, 2 of which were invasive; the earliest tumor appeared 8.5 months after initiation of the carcinogenic diet. None of the rats given a pyridoxine-deficient diet alone developed bladder tumors, and none of the rats given cyclophosphamide with a normal diet developed bladder tumors. Carcinoma *in situ* was not observed to precede the development of invasive carcinomas, although the epithelium of the bladder adjacent to already-developed carcinomas showed carcinoma *in situ*. During the first 6 months after initiation of the carcinogenic diet, rats given cyclophosphamide showed epithelial hyperplasia in the bladder. Papillomas developed after 4 months on the carcinogenic diet, and after 6 months squamous metaplasia were observed. Tumor formation was not influenced by dosage of cyclophosphamide or by the timing of the start of the carcinogenic diet. Synergism between cyclophosphamide and the known immunosuppressive effects of FAA may have been active in the production of bladder carcinoma in the carcinogenic diet group.

- 1303 THE EFFECT OF L-ASPARAGINASE ON MITOTIC ACTIVITY DURING N-2-FLUORENYLACETAMIDE HEPATOCARCINOGENESIS: SUBPOPULATIONS OF NODULAR CELLS. (E.) Becker, F. F. (New York U. Sch. Med., New York) and K. M. Klein. *Cancer Res* 31(2):169-173, 1971.

Administration of L-asparaginase (100 IU/kg) to 70%-hepatectomized rats fed for 3 wk on a diet of 0.06% N-2-fluorenylacetylamide (2-FAA) diminished the increased mitotic activity of liver cells and hepatic nodules which followed hepatectomy. At the end of 4 cycles of 2-FAA feeding, livers of rats showed a 75% conversion to hyperplastic nodules. Following hepatectomy, mitotic activity measured by ^3H -thymidine incorporation increased 44-fold in liver tissue apparently due to increased DNA synthesis in hepatocytes. Seventy percent hepatectomy increased ^3H -thymidine incorporation 100-fold in hyperplastic hepatic nodules. L-asparaginase completely inhibited ^3H -thymidine incorporation in normal hepatocytes after hepatectomy, and decreased by 80% thymidine incorporation in nodular hepatocytes. L-asparaginase delayed the mitotic cycle of normal hepatocytes by 10-12 hr. Aggregates of cells within the hyperplastic nodules were found to resist the effects of L-asparaginase.

- 1304 STUDIES OF EXPERIMENTAL BLADDER CARCINOMA IN FISCHER 344 FEMALE RATS: II. CHARACTERIZATION OF 3 CELL LINES DERIVED FROM INDUCED URINARY BLADDER CARCINOMAS. (E.) Lavin, P. (Dept. Biol., Massachusetts Inst. Tech., Cambridge) and L. G. Koss. *J Nat Cancer Inst* 46(3):597-614, 1971.

Two epithelial and 1 fibroblastic cell lines derived from urinary bladder squamous carcinomas which had been induced in rats by N-2-fluorenylacetylamide and cyclophosphamide were maintained *in vitro* through multiple passages. In one of the epithelial cell lines (BC₆) fibroblasts comprised part of the culture in early passages; however fibroblasts were supplanted by epithelial cells after the third passage. Both epithelial cell lines produced carcinomas in the cheek pouches of hamsters and in newborn rats; tumors were undifferentiated carcinomas and well-differentiated squamous carcinomas. Fibroblast cells did not produce tumors in hamsters or rats. Although the fibroblast line was initially diploid, all three lines became 50-80% tetraploid after 15-18 passages. Marker chromosomes were common in the epithelial cell lines. Electron microscopy showed that 1 of the epithelial cell lines was marked by cytoplasmic tonofibrils forming numerous microvilli; these cells had abundant desmosomes and many free ribosomes. Cells in this line showed differentiation *in vitro* similar to that observed in keratinizing squamous epithelium *in vivo*; however, fully keratinized cells were not seen. Many degenerating cells in this line had an electron-dense membrane measuring 175-200 Å located beneath the plasmalemma and apparently fused to its inner leaflet. Numerous intracytoplasmic vesicles were seen resembling those seen in superficial cells of the rat urinary bladder; vesicles were seen in epithelial cells of one line *in vivo* and in cheek pouch tumors produced by these cells in hamsters. The other epithelial line and the fibroblastic cell line were morphologically different from the differentiating epithelial cell line, having few microvilli and lacking cytoplasmic vesicles and may have originated from cells of a different type.

- 1305 STUDIES ON LIVER PLASMA MEMBRANES OF RATS FED N-2-FLUORENYLACETAMIDE. (E.)

Chandrasekhara, N. (Central Food Technol. Res. Inst. Mysore, India) and K. A. Narayan. *Cancer Res* 30(12):2876-2880, 1970.

This study was designed to investigate the lipid composition of liver plasma membranes of male weanling rats fed N-2-fluorenylacetylamide (0.05 or 0.3 g/kg diet) using marker enzymes, 5'-nucleotidase and Mg^{2+} -Na-K-ATPase. Specific activities of 5'-nucleotidase and ATPase were lower in liver homogenates of N-2-fluorenylacetylamide-fed rats than in normal liver homogenates. Membranes from both preneoplastic and neoplastic livers had markedly low 5'-nucleotidase activity but showed no change in ATPase activity. Glucose 6-phosphatase activity was quite low in membranes from all groups while there was a marked increase in the percentage of total phospholipids in membranes from both preneoplastic and neoplastic livers ranging from 71.4-79.3% compared to 59.3% in normal membranes and only a nominal increase in liver homogenates ranging from 60.3-66.5% compared to 57.7% in homogenates from normal livers. Carcinogenesis did not change the percentage of cholesterol in membranes with a slight increase noted in the carcinogenic liver homogenates from 6.8% to 8.0% compared to 5.5% for normal liver homogenates. A significant increase ($p < 0.05$) in total polyunsaturated fatty acids and a corresponding decrease in total saturated fatty acids was seen in membranes from N-2-fluorenylacetylamide-fed rats compared to fatty acid composition in membranes from normal rats. The floating layer was increased 5- to 10-fold in carcinogenic liver homogenates and was characterized by fairly high activities of 5'-nucleotidase and ATPase and low activities of glucose-6-phosphatase and succinic dehydrogenase with lipid:protein ratios higher and phospholipid fraction lower compared to normal liver homogenates. Increased yield of plasma membranes and floating fractions may be due to the presence of increased quantities of membrane precursors.

- 1306 INSTABILITY OF FLUORENYLAMINE-SUBSTITUTED POLYNUCLEOTIDES: LOSS OF CARCINOGENIC ACTIVITY IN THE PRODUCTION OF AN ALTERED NUCLEIC ACID. (E.) King, C. M. (Michael Reese Hosp. Med. Ctr., Chicago, Ill.) and B. Phillips. *Chem Biol Interact* 2(3):267-271, 1970.

The instability of fluorenylamine-substituted rat liver RNA, calf thymus DNA and poly-G on incubation in 0.5 M Tris-HCl at physiological temperature and pH were studied. Substituted rat liver ribosomal RNA exhibited the greatest instability, while substituted calf thymus DNA appeared to be the most stable. The guanylic acid content of substituted sRNA at the start of incubation showed a 19% loss compared to control preparations of unmodified sRNA; no restoration of guanylic acid content occurred after incubation despite a 78% loss of absorbance at 320 mμ, which indicated a loss of fluorene residues.

dues. Loss of fluorene residues from nucleic acid adducts may be due to preferential release of fluorenylamine substituents, and lack of restoration of guanylic acid content with release of fluorene residues may represent a mechanism by which release of bound carcinogen damages nucleic acid. The adenine, cytosine or uracil contents of sRNA were not altered by the reagent which was used to make the fluorenylamine derivatives or by the incubation conditions.

- 1307 CELL PROLIFERATION IN THE THYMUS AFTER REPEATED SUBCUTANEOUS ADMINISTRATION OF FREUND'S ADJUVANT. (Ger.) Backmann, B. (Path. Inst. U. Munster, Germany) and K. Morgenroth, Jr. *Verhandl Deutsch Ges Path* 54:243-247, 1970.

Repeated s.c. injections of Freund adjuvant in the neck of a guinea pig produced an interstitial pulmonary fibrosis in the presence of an interstitial pneumonia of the plasmacellular histiocyte type. No other organs revealed any cellular reactions, except the thymus, in which there was proliferation of the lymphoid and reticular cells. It was possible to measure by autoradiography the proliferation of the lymphoid cells and of the small and large reticular cells, using as a measure of activity the ^3H index 1 hr after the administration of ^3H -thymidine. The lymphoid cell index rose from 1.9% (in controls) to 5.7% 11 days after the administration of the adjuvant and to 6.4% 22 days after the adjuvant. Proliferation increase in small reticular cells was 1.4 times the control value after 11 days, and 4.2 times greater 22 days after the adjuvant. The large reticular cells showed a lesser activity by an increase of only 1.2-fold after 11 days and 1.5-fold after 22 days. The selective immunological reaction of the thymus and the lungs is probably explainable by the mainly lymphogenic transport of the antigen reactive substances of Freund adjuvant.

- 1308 AFLATOXIN STRUCTURE AND HEPATOCARCINOGENICITY IN RAINBOW TROUT (*SALMO GAIARDNERI*). (E.) Ayres, J. L. (Cotton Producers Ass., Atlanta, Ga.), D. J. Lee, J. H. Wales and R. O. Sinnhuber. *J Nat Cancer Inst* 46(3):461-564, 1971.

One yr after introduction of dietary aflatoxin B_1 (4 parts per billion, ppb) 25% of the rainbow trout developed hepatomas compared to 0% of the controls not given the carcinogen. At 16 months the hepatoma incidence in these fish was 35%. Eight ppb of aflatoxin B_1 produced tumors in 70% of the fish at 1 yr, while 4 ppb aflatoxin B_1 together with 4 ppb aflatoxin B_2 gave a 43% tumor incidence at 1 yr (70% at 16 months). Twenty ppb aflatoxin B_1 caused a tumor incidence of 78% in 1 yr; however, the same amount of aflatoxin B_2 produced a tumor incidence of only 5%. Aflatoxin G_1 (20 ppb) caused tumors in 5% of fish, while aflatoxin G_2 , 7-ethoxy-4-methylcoumarin, and isobergaptene (all at 20 ppb) produced no tumors in trout. Tetrahydrodeoxoaflatoxin B_1 (20 ppb) resulted in a 1% tumor incidence, and 5,7-dimethoxycyclopentenone-(2,3-c)coumarin produced no tumors. These results suggested that the carcinogen-

icity of aflatoxin B_1 depended on the bifunctional activity of the molecule with a requirement for both the dihydrofurofuran ring system and the unsaturated δ -lactone moieties.

- 1309 SPECIES DIFFERENCES IN THE *IN VITRO* METABOLISM OF AFLATOXIN B_1 . (E.) Bassir, O. (Biochem Dept., U. Ibadan, Nigeria) and P. O. Emafo. *FEBS Letters* 12(5):273-275, 1971.

The *in vitro* metabolism of aflatoxin B_1 was investigated in liver microsomes prepared from toad, lizard, duck, and cockerel. Liver microsomes and the soluble fraction of the liver were incubated with 160 nmoles of aflatoxin B_1 . Lizard and toad liver microsomes, but not duck or cockerel microsomes, metabolized aflatoxin B_1 into a blue-violet fluorescing substance of R_f 0.20 in a 10% acetone in chloroform solvent system. This metabolite was identified as aflatoxin M_1 . The presence of the aflatoxin M_1 metabolite in lizard and toad liver, and its absence in duck and cockerel liver, indicated a species difference in the metabolism of aflatoxin B_1 by hydroxylation to aflatoxin M_1 . Another metabolite of zero R_f value in the same solvent system was produced by all the animal species studied. Of the total aflatoxin B_1 in the incubation media, 98-99% was metabolized in the first 1 hr of incubation. In duck and cockerel, differences in the metabolism of aflatoxin B_1 were not pronounced, suggesting that factors other than metabolism account for differences in susceptibility in these species.

- 1310 AFLATOXIN P_1 : A NEW AFLATOXIN METABOLITE IN MONKEYS. (E.) Dalezios, J. (Dept. Nutr. Food Sci., Massachusetts Inst. Tech., Cambridge), G. N. Wogan and S. M. Weinreb. *Science* 171(3971):584-585, 1971.

A new metabolite of aflatoxin B_1 was isolated from the urine of rhesus monkeys which had been administered aflatoxin B_1 and was designated aflatoxin P_1 . Aflatoxin P_1 was the metabolic product of O-demethylation of aflatoxin B_1 ; 50% of it was present in the monkey urine as the glucuronide, 10% as the sulfate and 3% as the phenol. It appears to be the major urinary metabolite of aflatoxin B_1 and represents 20% of the excreted form of a single dose within 24 hr after injection.

- 1311 EFFECT OF AFLATOXIN ON CARBOHYDRATE METABOLISM IN CHICK LIVER. (E.) Shankaran, R. (Dept. Psychiat., U. British Columbia, Vancouver, Canada), H. G. Raj and T. A. Venkitesubramanian. *Enzymologia* 39(6):371-378, 1970.

Carbohydrate metabolizing enzymes were assayed in the livers of male chicks given i.p. injections of aflatoxin B (2.7 mg/kg) 48 hr before sacrifice. A significant decrease in the activity of uridine diphosphate glucose-glycogen transglucosylase was found in the treated birds. Control values for specific glycogen synthetase activity were 4.05 U/g

protein, while glycogen synthetase activity in aflatoxin-treated birds was 0.44 U/g. Glycogen phosphorylase specific activity was decreased from 155 U/g in controls to 62 U/g in treated chicks. Control and aflatoxin-treated values for phosphoglucose mutase specific activity were 854 and 670 U/g, resp. Glucose-6-phosphatase specific activity in controls and aflatoxin-treated birds was 40 and 8.16 U/g, resp. Activity of hexose monophosphate dehydrogenases were elevated 3-fold in aflatoxin-treated birds over controls.

- 1312 *IN VITRO* MALIGNANT TRANSFORMATION OF CELLS DERIVED FROM RAT LIVER BY MEANS OF AFLATOXIN B₁. (E.) Toyoshima, K. (Nara Med. Coll., Japan), Y. Hiasa, N. Ito and Y. Tsubura. *Carcinogenesis* 61(6):557-561, 1970.

Transformation of rat liver cells by aflatoxin B₁ was investigated in cells cultivated through 12 subcultures for 161 days and exposed to aflatoxin B₁ (0.01-10 ppm) for 5-7 days. Morphological transformation was observed in all cell cultures exposed to aflatoxin B₁ and was most conspicuous at 2 wk after exposure. Approximately $4-5 \times 10^4$ transformed cells which were back-transplanted into newborn rats produced fibrosarcomas in 10 of 39 rats after latency periods of 75-187 days. Aflatoxin B₁ appeared to be a relatively potent carcinogen *in vitro* and able to cause moderate transformation in varying concentrations.

- 1313 INHIBITORY ACTION OF PREGNENOLONE ON LIVER CARCINOGENESIS AND ENHANCEMENT OF THE DEVELOPMENT OF TUMORS IN THE INTERSTITIAL TESTICULAR GLAND IN RATS TREATED WITH PARA-DIMETHYLAMINOAZOBENZENE (DAB). (Fr.) Lacassagne, A. (Fac. Med. Paris, France), M. F. Jayle and L. Hurst. *C R Acad Sci* 272(1):174-177, 1971.

Comparison of the effects of various C-21 steroids in the production of hepatic carcinomas in male rats given DAB daily (600 mg/kg) has demonstrated that progesterone (Δ_4 -P) and 17 α -hydroxyprogesterone (17-OH- Δ_4 -P) retarded the process of cancerization of the liver by DAB, and that pregnenolone (Δ_5 -P) and 17 α -hydroxypregnenolone (17-OH- Δ_5 -P) inhibited it completely. One of 3 rats given progesterone developed hepatoma, while 3 of 6 rats given 17-OH- Δ_4 -P developed hepatomas; none of the 20 rats given pregnenolone or 17-OH- Δ_5 -P developed hepatomas. In addition, early-stage tumors of the Leydig cells were found in 1 rat receiving Δ_5 or 17-OH- Δ_5 -P with DAB. The development of the Leydig cell tumors may have been influenced by the hypothalamic area where the hypophyseal tropic hormone is elaborated.

- 1314 THE EFFECT OF THE HORMONAL BALANCE ON *p*-DIMETHYLAMINOAZOBENZENE HEPATOCARCINOGENESIS IN RATS. (Rus.) Podzey, L. K. (P. A. Herzen Inst. Oncol. Moscow, U.S.S.R.). *Russkaya Fiziol Eksp Ter* 14(6):32-36, 1970.

p-Dimethylaminoazobenzene (DAB) hepatocarcinogenesis in conditions of castration, synestrol or testosterone treatment was investigated in male and female Wistar rats maintained on a rice and carrot diet. The following experimental groups were used: I) 46 males and 50 females received no treatment and were maintained on a normal diet; II) 47 males and 46 females were maintained on a rice and carrot diet; III) 47 males and 46 females were on the group II diet and treated with DAB (6 mg p.o. daily for 10 months); IV) 55 males and 54 females were treated with DAB as above following castration; V) 59 males and 63 females were treated the same as group IV and given synestrol (s.c. implant of 30 mg synestrol followed 1 month later by s.c. injections of 0.05 mg synestrol on alternate days for the duration of the experimental period); VI) 55 males and 56 females were treated the same as group V but received testosterone instead of synestrol. Group V showed the most severe DAB-induced effects with hepatomas occurring in 17% of the female rats and in 22% of the male rats after latency periods of 5-6 months. Group VI had the lowest tumor incidence (3.5-3.6%) after a latency period of 9-10 months. Group IV had a 5.5% tumor incidence in females and 27% tumor incidence in males after 8-9 months of latency. Group III had a tumor incidence of 10.5% in females and 6.7% in male rats after 6 and 9 months of latency, resp. No tumors were observed in Groups I or II.

- 1315 THE EFFECT OF THE ADMINISTRATION OF *N,N*-DIMETHYL-4-AMINOAZOBENZENE (DAB) ON THE ACTIVITY OF DAB-REDUCTASE AND NADPH-CYTOCHROME *c* REDUCTASE. (E.) Ketterer, B. (Middlesex Hosp. Med. Sch., London, England), P. Ross-Mansell and H. Davidson. *Chem Biol Interact* 2(3):183-194, 1970.

The effect of *N,N*-dimethyl-4-aminoazobenzene (DAB) on the activity and cellular distribution of DAB-reductase and NADPH-cytochrome *c* reductase was investigated in male rats given 50 mg DAB by i.p. injection or 0.06% DAB in the diet. One hr after injection of DAB, a significant decrease in DAB-reductase was observed in rat livers; DAB-reductase values for untreated controls were 236 μ moles DAB reduced/min/100 mg microsomal protein, while in rats injected with DAB, reductase values 1 hr postinjection were 111 μ moles/min/100 mg. About 6-16 hr postinjection, DAB-reductase values in treated rats reached their nadir (0 at 6 hr, 63 μ moles/min/100 mg at 16 hr); DAB-reductase values recovered steadily after 16 hr. In chronic DAB feeding studies, it was found that the smooth microsomes in normals contained more than twice the concentrations of DAB-reductase than the rough microsomes. The decrease in DAB-reductase activity caused by DAB had the effect of equalizing the concentrations of DAB-reductase in the smooth and rough microsomal fractions, with the rough microsomes having slightly higher concentrations of DAB-reductase than the smooth. The addition of flavin adenine nucleotide to the assay mixture only increased DAB-reductase activity from 63 to 96 μ mol/min/100 mg in treated animals, indicating that reduced DAB-reductase activity was not due to reduced levels of flavin. DAB had no effect on NADPH-cytochrome *c* activity which had the same distribution

pattern as the residual DAB-reductase (higher concentrations in the rough than in the smooth microsomes). DAB-reductase activity may involve 2 components, one which is sensitive to DAB toxicity, and one which is unaffected by DAB and involves the NADPH-cytochrome *c* reductase flavoprotein.

316 INHIBITION BY CHLORAMPHENICOL OF AMINOAZO DYE CARCINOGENESIS IN RAT LIVER: STUDIES OF BIOCHEMICAL CHANGES IN RAT LIVER AND PROTEIN BINDING OF CARCINOGEN. (E.) Blunck, J. M. (Path. Dept. Melbourne, Parkville, Australia). *Chem Biol Interact* 2(3):217-228, 1970.

The protein-bound dye content of the livers of rats fed carcinogens and chloramphenicol, a compound known to inhibit hepatocarcinogenesis in rats, was determined. Rats were given diets containing either 3'-methyl-4-dimethylaminoazobenzene (3'MeDAB) in 0.06% concentration with and without 2% chloramphenicol. No significant differences could be detected between protein-bound dye in livers of chloramphenicol-treated rats and livers of untreated rats. Rats given both 3'MeDAB and chloramphenicol showed greater increases in liver size than rats in other groups. In rats given a diet containing chloramphenicol, liver DNA content after 20 days of the diet was 36.13 mg/100 g body wt, and control liver RNA was 28.30 mg/100 g. Total liver protein also increased in rats given chloramphenicol, and liver DNA was increased in rats given 3'MeDAB-containing diets. In rats given chloramphenicol, the RNA to DNA ratio increased, while in rats given 3'MeDAB alone this ratio decreased; in controls and in rats given both compounds, the ratio remained normal. This observed disturbance of the normal RNA-DNA ratio may be causally connected with 3'MeDAB hepatocarcinogenesis in the rat.

317 ABNORMAL SIZE PROFILES OF SOLUBLE MACROMOLECULES FROM AZO-DYE LIVER TUMORS. (E.) Korof, S. (Inst. Cancer Res., Fox Chase, Philadelphia, Pa.), E. M. Young, R. Z. McBride and C. B. Coffey. *Nat Cancer Inst* 46(2):275-280, 1971.

Male rats were fed for 17-27 wk on a diet containing 0.058% 3'-methyl-4-dimethylaminoazobenzene (3'-MeDAB); at the end of the feeding period the rats were killed, and the primary liver tumors induced by the carcinogen were prepared for sieving through long gel columns to determine the relative sizes of the soluble macromolecules they contained. Soluble macromolecules were also examined in livers of control rats and in preneoplastic liver tissue from rats given 3'-Me-DAB. Primary liver tumors as well as other tissues yielded soluble macromolecules in size, ranging from 2S to 15-20S; in both control and normal tissues, macromolecule size profiles appeared to break down into discrete and clearly distinguished categories, but the sizes of tumor macromolecules were distributed in diffuse profiles. The 15-20S component was present in greatest abundance (34%) in tumor extracts, but constituted only 10% of the macromolecules for normal liver tissue. The relative amount of 6-7.5S macromolecule in tumor extracts was half that in normal liver tissue. The relative

proportions of many cellular proteins appeared to change following transformation of liver cells to tumors.

1318 PHOSPHOFRUCTOKINASE ACTIVITY AND RATE OF GLYCOLYSIS IN RAT LIVER DURING CARCINOGENESIS. (Rus.) Rubenchuk, B. L. (Inst. Nutr. Hygiene, Kiev, U.S.S.R.) and A. S. Petrun. *Bull Eksp Biol Med* 71(1):68-70, 1971.

Phosphofructokinase activity and the rate of glycolysis in rat liver during *p*-dimethylaminoazobenzene (DAB) carcinogenesis were investigated. A maximum of glycolytic activity (70 mg lactic acid/g protein as compared to 20 mg lactic acid/g protein in controls at 37°C) and a maximum of phosphofructokinase activity (20 μ M NADH/min/g at 25°C, 8 μ M NADH/min/g in controls) were noticed 18 wk after the beginning of the experiment before the occurrence of tumors. When assayed at the time of its maximal activity, phosphofructokinase revealed highest activity using 0.2 mM ATP levels in the presence of 5 mM of $MgCl_2$ and 20 mM of KCl. Its susceptibility towards ATP inhibition decreased in tissue of animals treated with DAB: no phosphofructokinase inhibition occurred with 6 mM of ATP which caused 72% inhibition in control tissue; citrate (5 mM) with ATP (4 mM) inhibited the enzyme by 85% in control tissue and by 36% in the experimental tissue. Enhanced formation of fructose-1,6-diphosphate (200%) coincided with the decrease of the susceptibility of phosphofructokinase towards ATP inhibition. DAB or its metabolites seem to interfere with the allosteric regulators of phosphofructokinase.

1319 ANILINE-INDUCED CHANGES IN THE CORPORA LUTEA OF RATS. (E.) Hatakeyama, S. (Inst. Med. Exp. Surg., U. Montreal, Quebec, Canada), K. Kovacs, E. Yeghiayan and J. A. Blascheck. *Amer J Obstet Gynec* 109(3):469-476, 1971.

Rats were given s.c. injections of 50 mg aniline for 7 consecutive days, killed, and their corpora lutea sectioned for electron microscopy. Aniline-treated corpus luteum cells showed marked intracellular lipid storage with swollen cells displaying either a clear or a foamy cytoplasm. A slight inflammatory reaction was occasionally seen, which consisted of polymorphonuclear leukocytes and mononuclear cells. Multiple theca cell nests, consisting of cells undergoing atrophy, were seen throughout the ovarian stroma. Most lipid-bearing cells in the aniline-treated cells showed no activity of steroid-3 β -ol-dehydrogenase. Succinic dehydrogenase activity was similar in treated and in untreated rats. The fine structure of the mitochondria remained intact in aniline treated rats, but the endoplasmic reticulum decreased markedly and in some cases was entirely absent, suggesting depleted steroidogenesis. Aniline apparently interfered with steroid synthesis in the corpus luteum.

1320 THE BINDING OF ORTHO-AMINOAZOTOLUENE IN PROLIFERATING TISSUES. (E.) Lawson, T. A. (U. Queensland Sch. Med., Herston, Australia)

and F. K. Dzhiyev. *Chem Biol Interact* 2(3):165-174, 1970.

The extent of binding of *ortho*-aminoazotoluene (*o*-AAT) to mouse liver DNA, RNA and protein at various times after partial hepatectomy was investigated; binding of *o*-AAT to mouse-bladder DNA was also investigated in untreated mice and in mice whose bladders contained an implanted glass bead. The level of DNA synthesis in the regenerating liver of partially hepatectomized mice was measured by incorporation of 6-³H-thymidine. By 42-48 hr after hepatectomy, the activity of newly synthesized DNA was 3000 dpm/μg deoxyribose; at 60-66 hr, DNA activity was at 3600 dpm after an intervening drop. The administration of 12 μg *o*-AAT did not affect DNA synthesis in the regenerating liver. A period of increased mitosis was seen in the regenerating liver cells corresponding to the 48 hr maximum recorded for DNA synthesis; at 56 hr the mitotic index was 5; the administration of *o*-AAT did not affect the levels of mitosis in the regenerating cells. The 66 hr maximum for DNA synthesis was followed by a period of poorly synchronized mitosis. The binding of tritiated *o*-AAT to liver nucleic acids and protein in hepatectomized mice resembled the pattern of its binding to liver nucleic acids of intact mice during periods of maximal DNA synthesis and during the period of poorly synchronized mitosis. Binding of *o*-AAT to DNA was increased 6-fold over its normal level during the 56 hr maximum period of mitosis. DNA synthesis in livers of mice undergoing bile duct ligation increased 2-fold over a period of 24 hr; however, bile duct ligation did not affect binding of *o*-AAT to DNA. A 2-fold increase in bladder DNA synthesis also occurred in mice bearing a luminary glass bead in their bladders, but *o*-AAT binding to DNA was unaffected by implantation of the foreign body.

1321 THE LOCALIZATION OF PHORBOL ESTER ¹⁴C-ACETATE IN PAPILLOMAS THAT WERE INITIATED WITH 7,12 DMBA AND PROMOTED WITH PHORBOL ESTER: AN ELECTRON MICROSCOPIC AUTORADIOGRAPHY STUDY. (E.) Bogart, B. (New York U. Med. Ctr., New York, N. Y.), L. Prutkin and P. R. Ocken. *J Invest Derm* 56(2):140-146, 1971.

The tumor enhancing activity of phorbol ester at the cellular level has been studied in female H-ICR mice with ¹⁴C-acetate. In mice pretreated with 7,12-dimethylbenz(a)anthracene (DMBA), the 1st papillomatous growth in response to phorbol ester acetate treatment occurred within 43 days with a yield of 2-5 tumors per animal and ranging in size from 0.25 to 0.5 cm in height. Phase microscopy revealed epithelial hyperplasia of the strata spinosum and granulosum with enlargement of the intercellular spaces in the strata basale and spinosum; extensive numbers of free ribosomes and polysomes were present within the cytoplasm of the cells of these two layers. Tonofibrils, sparse rough endoplasmic reticulum, Golgi apparatus, and chromatin material diffusely scattered throughout the nuclei, which contained 1-3 enlarged nucleoli, were also

noted. Control animals receiving either DMBA or phorbol ester acetate solely developed no papillomatous growths. Phorbol ester acetate appears to gain entrance into the cell as a metabolite which retains the ¹⁴C label.

1322 RADIOAUTOGRAPHIC ANALYSIS OF 7,12-DIMETHYLBENZ(a)ANTHRACENE-³H INCORPORATION AND CELL SURVIVAL OF SYRIAN HAMSTER EMBRYO CELLS DURING EXPOSURE TO NUCLEIC ACID INHIBITORS. (E.) Connell, D. I. (Chester Beatty Res. Inst., London England), L. A. Riechers and J. A. DiPaolo. *J Natl Cancer* 46(1):183-193, 1971.

Alteration by nucleic acid inhibitors of 7,12-dimethylbenz(a)anthracene (DMBA) binding *in vitro* to Syrian hamster 14-day embryo cells, and the effect of inhibitors on DNA and RNA synthesis were demonstrated through radioautographic techniques. Toxicity within the first 12 hr of continuous exposure of culture to DMBA did not indicate a dose response but after 72 hr of treatment with 0.01, 0.04, 0.06, or 0.10 μg DMBA/10⁵ cells, cell survival was 82, 52, 29 and 14%, resp., relative to controls. Seven hr of treatment with 0.01 μg DMBA resulted in survival of 75% of the cells, and cell survivals approximated 80% with 0.04 μg. With concentrations of 0.04 μg DMBA/10⁵ cells, both the percentage of labeled cells and the amount of label incorporated per nucleus increased with length of exposure; the rate of incorporation inversely related to the doubling time of individual cultures, and incorporation of either uridine-³H or thymidine-³H was similar for treated and untreated cells. Hydroxyurea induced a transitory inhibition of thymidine-³H incorporation which was dose-dependent and which was greatest during exposure to 152 μg hydroxyurea/10⁵ cells; the percentage of treated cells that incorporated label after 30 min to 76 μg exposure was 21, while that of controls was 36; however, after 12 hr exposure to the inhibitor, the percentage of cells that incorporated thymidine-³H exceeded control number. Actinomycin D inhibited 60% of the cells binding DMBA-³H with approximately a 60% loss of label, although the level of RNA synthesis returned to normal after 12 hr of incubation; DNA synthesis fell off to less than 40% of control. Actinomycin D and 2-mercapto-1-(β-4-pyridethyl)benzimidazole inhibited DMBA-³H incorporation into the nucleus while hydroxyurea and excess thymidine had no effect. A significant depression in the multiplication of treated cells and a loss of cells followed exposure to any of the inhibitors.

1323 EXPERIMENTAL CANCER OF THE UTERINE CERVIX OF MICE AND RATS: A HISTOLOGICAL AND HISTOCHEMICAL STUDY. (E.) Stenbäck, F. (Dept. Pathol. U. Oulu, Finland). *Ann Med Exp Biol Fenn* 48(4):201-211, 1970.

The development and preliminary stages of carcinogenesis induced histochemical changes in the uterine cervix of 30 NMRI mice and 30 Sprague Dawley rats were studied using 1% 7,12-dimethylbenz(a)anthracene (DMBA) in acetone. In dysplastic epithelium increased amounts of Gram-staining material, disulfide groups, RNA and acid mucopolysaccharides, marked inflammation

reaction and increased numbers of mast cells in sub-epithelial tissues and decreased glycogen content were noted. One carcinoma *in situ* was distinguished by well-differentiated tumor cells tending toward keratinization, high alkaline and acid phosphatase and adenosine triphosphatase activities, regular distribution of oxidative enzymes, connective tissue proliferation and inflammatory reaction in the stroma. A second type was composed of anaplastic cells showing increased lactate dehydrogenase activity, weak phosphatase activity and irregularly distributed oxidative enzyme activity and degeneration of stromal collagen and elastic fibers. With rats, some sarcomas developed originally in cervical connective tissue characterized by fusiform cells of varying degrees of pleomorphism. Correlation of histological progression of neoplastic transformation with histochemical properties of tissue was not adequate for identification of definitely malignant states.

- 1324 DELAYED HYPERSENSITIVITY INDUCED IN GUINEA PIGS BY 7,12-DIMETHYLBENZ(a)ANTHRACENE. (E.) Burger, D. R. (VA Hosp., Portland, Ore.), L. E. Irish, R. M. Vetto and D. J. Hinrichs. *Infect Immun* 3(3):478-480, 1971.

Contact sensitivity elicited in the epidermis of guinea pigs by topical applications of 7,12-dimethylbenz(a)anthracene (DMBA) was investigated. Guinea pigs were presensitized to the carcinogen by applications of a 2% solution of DMBA daily for 7 days; 5 days after sensitization, the animals were skin tested for sensitivity by applications of 1%, 0.5%, and 0.1% DMBA solutions or 1% solutions of benzpyrene, benzan-thracene, or methylcholanthrene. In all guinea pigs reactions typified by homogeneous erythema and induration were observed at the skin test sites 24 and 48 hr after testing with 1% DMBA. Similar reactions were observed after skin testing with benzan-thracene and benzpyrene, but not after methylcholanthrene skin testing. Mononuclear cell infiltration at the skin test site was observed 24 and 48 hr after skin testing, and suprascapular lymph nodes draining the treatment site showed increased numbers of immunoblasts. The sensitivity was transferable by injection of other guinea pigs with peritoneal exudative cells, lymph node cells, and serum from sensitive animals. Contact sensitivity to DMBA was retained for at least 1 yr, during which time none of the sensitized animals developed tumors.

- 1325 EFFECT OF HETEROLOGOUS ANTITHYMOCYTE SERUM ON MOUSE SKIN TUMORIGENESIS. (E.) Haran-Ghera, N. (Weizmann Inst. Sc., Rehovoth, Israel) and M. Lurie. *J Nat Cancer Inst* 46(1):103-112, 1971.

The effect of transient immune impairment on the initiation and promotion phases of skin tumorigenesis was studied by the 2-stage induction method utilizing heterologous antithymocyte serum (ATS) in SWR inbred female mice. Three days after the second of 2 s.c. injections of ATS, tumorigenesis was initiated with a single application of a 1.5% soln of 7,12-dimethylbenz(a)anthracene (DMBA) followed 1 wk later by bi-weekly applications of 5% croton oil for 30 wk; 2 control groups, one with normal rabbit serum in place

of ATS and one without any serum treatment, were used. The first papillomas occurred 5-6 wk later, and by the 10th wk 70-85% of the mice developed an average of 2.5-3.7 papillomas each. Concurrent treatment with ATS during promotion resulted in the appearance of 14-16 papillomas/mouse at 30 wk with no regression at the end of 15 wk following termination of croton oil promotion in contrast to regression in both control groups at this time. Malignant tumors occurred in 33% of the ATS and croton oil-treated mice with an average latent period of 161-201 days. When ATS was injected late in the promotion phase, progression from benign tumors to malignant squamous carcinomas was enhanced with the incidence in the ATS-treated group being 41% compared to 14% in the controls. On the basis of present results, it is doubtful whether the reported suppressive effect of poly I·poly C on DMBA tumorigenesis is mediated through its effect on host immunity.

- 1326 MALIGNANT TRANSFORMATION INDUCED BY 7,12-DIMETHYLBENZ(a)ANTHRACENE IN RAT EMBRYO CELLS INFECTED WITH RAUSCHER LEUKEMIA VIRUS. (E.) Rhim, J. S. (Microbiol. Assoc., Bethesda, Md.), W. Vass, H. Y. Cho and R. J. Huebner. *Int J Cancer* 7(1):65-74, 1971.

Rat embryo cells were infected with Rauscher leukemia virus and treated for 7 days with 7,12-dimethylbenz(a)-anthracene (DMBA 0.01-0.5 µg/ml) to investigate the changes produced in the infected cells by treatment with the carcinogen. In the DMBA-treated and virus-infected cells, morphological alterations of cells and an abnormal pattern of growth were noted 42-45 days after DMBA treatment; similar changes were not seen in uninfected cells treated with DMBA. Uninfected cells treated with DMBA and virus-infected cells not treated with DMBA failed to show any evidence of transformation. Infected DMBA-treated cells showed foci of transformed cells consisting of randomly arranged, criss-crossing spindle-shaped cells. Large cells with atypical nuclei were also observed. The DMBA-treated infected cells had a growth rate 3 times that of virus-infected untreated cells; DMBA treatment inhibited the growth of cells not infected by virus. S.C. sarcomas developed when virus-transformed cells were injected into newborn rats; however, no tumors resulted from injection of infected cells or DMBA-treated untransformed cells. Tumor cells in culture produced group-specific complement fixing antigens characteristic of the murine leukemia-sarcoma viruses and the C-type RNA virus particles. Both DMBA and virus appeared to be necessary for transformation of the rat embryo cells; the viral genome may have provided information for malignant transformation by DMBA.

- 1327 BIOCHEMICAL EVENTS ASSOCIATED WITH REGRESSION OF 7,12-DIMETHYLBENZ(a)ANTHRACENE-INDUCED MAMMARY CARCINOMAS AFTER OVARECTOMY. (E.) Hilf, R. (U. Rochester Sch. Med. Dent., N. Y.), H. Goldenberg, I. Michel, M. Gruenstein, D. R. Meranze and M. B. Shimkin. *Cancer Res* 31(1):52-58, 1971.

The biochemical changes occurring in mammary carcinomas induced in female rats by 7,12-dimethylbenz(a)-

anthracene (DMBA) during tumor regression following ovariectomy were investigated. Rats were given 5 mg DMBA by stomach instillation; at various times after the appearance of mammary tumors, rats were ovariectomized and sacrificed 1, 5 or 14 days later. No significant decrease in tumor size or volume occurred until 14 days after ovariectomy, at which time tumor size and volume had decreased 27% and 62%, resp. Tumors obtained 1 day after ovariectomy showed a 48% decrease in normal glucose-6-phosphate dehydrogenase activity, and a 34% decrease in cholesterol activity. Aspartate aminotransferase increased 72% in ovariectomized rats on day 1, and hexokinase had increased by 340%. By day 5 after ovariectomy there was a 32% decrease in the RNA to DNA ratio in the DMBA-induced tumors, a 49% decrease in phosphoglucumutase, a 61% decrease in glutamate dehydrogenase and a 33% decrease in pyruvate kinase activity. By 14 days after ovariectomy, NADP-malate dehydrogenase activity was reduced by 45%, and the RNA level was reduced 40%, and none of the altered parameters observed on earlier days had returned to normal levels. NADP-isocitrate dehydrogenase and glucose-phosphate isomerase were also altered on day 14, but DNA and free fatty acid were not affected by ovariectomy. Rats ovariectomized when their first DMBA-induced tumor had reached 2 x 2 cm and rats ovariectomized 35 days after their first tumor had reached 0.5 x 0.5 cm exhibited similar biochemical alterations.

- 1328 EFFECT OF PINEALECTOMY UPON MELANOID TUMORS IN THE GOLDEN HAMSTER INDUCED BY ORAL ADMINISTRATION OF A SINGLE DOSE OF 9,10-DIMETHYL-1,2-BENZANTHRACENE. (Fr.) Aubert, C. (Inst. Gustave-Roussy, Villejuif, France), M. Prade and C. Bohuon. *C R Acad Sci* 271(25):2465-2468, 1970.

The role of the pineal body was investigated in golden hamsters with melanoid tumors induced by the administration of 7,12-dimethylbenz(a)anthracene (DMBA). In the 2 groups of animals, intact and pinealectomized, the melanoid tumors appeared 4 months after the ingestion of DMBA. These were of variable size in the same animal, ranging from microscopic to 2-3 cm in diameter. Pinealectomy resulted in a considerable increase in the number of melanoid tumors, but did not alter the size or the histological character of the tumors; females had fewer tumors than males. The absence of the pineal body increased the tumorigenic effect of DMBA in the formation of melanoid tumors in the golden hamster, but this enhancement appears to be reduced by the female hormones. Whether the mechanism of action is entirely hormonal in nature or an immunologic response is still to be determined.

- 1329 RADIOLOGICAL AND MORPHOLOGICAL FEATURES OF CHEMICALLY-INDUCED OSTEOSARCOMAS IN CONDITIONS OF HYPERESTRINISM. (Rus.) Kornitsky, M. A. (Med. Inst. Orenburg, U.S.S.R.) *Vop Onkol* 16(12):44-49, 1970.

The morphological changes associated with the development of 7,2-dimethylbenz(a)anthracene (DMBA)-induced osteosarcoma in rabbits in conditions of

hyperestrinism was followed by roentgenology. Seventy female rabbits (5-7 months old) were implanted with a paraffin tablet containing 10 mg of DMBA in the proximal metaphysis of the tibia; 3 experimental groups were established: I) 20 rabbits received additional treatment; II) 40 rabbits were treated with a 2% oil solution of synestrol (0.2-0.3 ml twice a wk) starting 14 days after the implantation of the carcinogen; III) 10 rabbits were subjected to the same synestrol treatment starting 4 days after the implantation of the carcinogen. Roentgenologically detectable osteosarcoma developed in 10 of 20 rabbits of the Group I 193-210 days following carcinogen treatment. Eight rabbits of the group II developed 3 presarcomatous neoplasms: 3 small intramedullary sarcomas and 2 large osteosarcomas 220-430 days after carcinogen treatment. The rabbits of group III exhibited presarcomatous conditions in 3 cases 90-99 days after carcinogen implantation and actual sarcomas in 2 cases. The development of presarcomatous and sarcomatous regions occurred in conditions of diffuse bone demineralization caused by synestrol treatment. The presarcomatous alterations exhibited no specific roentgenological patterns in all the experimental animals. Development of osteosarcoma appeared roentgenologically as a fast growing enlargement of the surgical scar associated with the appearance of sclerotic foci around the scar, the destruction of the cortical layer and the neoplastic invasion outside the bone tissue in the rabbits of the Group I. The development of osteosarcoma in conditions of hyperestrinism presented specific roentgenological features such as repair processes within the metaphysis and sclerotic foci occurring much later than in the non-hormone-treated group. The developed tumors were morphologically classified as osteoid sarcoma, chondrosarcoma or polymorphic cell sarcoma. The morphology of osteoid fibrosarcomas revealed no destruction of the bone structures. Synestrol treatment decreased the incidence of induced osteosarcoma.

- 1330 SKIN TUMORIGENESIS IN MICE BY PETROLEUM ASPHALTS AND COAL-TAR PITCHES OF KNOWN POLYNUCLEAR AROMATIC HYDROCARBON CONTENT. (E.) Wallcave, L. (U. Nebraska Coll. Med., Omaha), H. Garcia, R. Feldman, W. Lijinsky and P. Shubik. *Toxic Appl Pharmacol* 18(1):41-52, 1971.

The tumorigenic effect of polynuclear hydrocarbon contained in petroleum asphalts and coal-tar pitch was investigated in mice given topical application of coal-tars and asphalts. Polynuclear aromatic hydrocarbons contained in the 2 media included coronene, picene, benzo(e)pyrene, chrysene, benz(a)anthracene and phenanthracene. Asphalt (2.5 mg) or coal-tar pitch (1.7 mg) was applied to a 1 square inch zone of the dorsal skin of adult mice twice a wk for periods up to 82 wk. Both coal tar and asphalt induced epidermal hyperplasia. Animals given asphalt frequently developed amyloidosis, particularly in the spleen and kidney. Coal-tar painted animals developed squamous cell carcinomas, benign squamous cell papillomas and keratoacanthomas. Carcinomas were developed by 31 coal-tar treated mice and by 2 asphalt-treated mice. In all, 91% of the

animals developed some form of skin tumor. Subcutaneous and internal tumors were observed in all treatment groups, including lung adenomas, malignant lymphomas, and endometrial carcinoma.

331 CHARACTERISTICS OF PRIMARY TUMORS INDUCED BY CARCINOGENIC POLYCYCLIC HYDROCARBONS IN SYRIAN HAMSTERS. (E.) DiPaolo, J. A. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), R. L. Elson and P. J. Donovan. *J Nat Cancer Inst* 46(1): 71-181, 1971.

Induction of primary tumors with a single s.c. injection of benzo(a)pyrene (0.1 µg) or 7,12-dimethylbenz(a)anthracene (0.1 mg) in Syrian hamsters and the characteristics of the cultures resulting from them are reported. Tumors were found only in the s.c. region of the groin at the site of inoculation and consisted of a single, firm encapsulated mass, easily removed from surrounding connective tissue and microscopically identifiable as fibrosarcomas; structurally different types were recognizable. The fibroid type with interlacing bundles oriented in many planes was very common; undifferentiated tumors showed considerable anaplasia and multilobulation with loose attachment to the skin and fascia, while mucoid mesenchymal tumors were characterized by active division and indistinct cellular boundaries. Primary tumors had common structural characteristics, whether induced with benzo(a)pyrene or 7,12-dimethylbenz(a)anthracene and secondary tumors resembled the parent tumor mass. Tumor cultures showed an increase in acid production, piling up of cells, general lack of cell orientation, and transformed colonies with tumorigenic potential were demonstrated with all culture lines. Chromosomal examination revealed 2 tumor lines with near-diploid modes, 1 with a diploid mode and 3 lines with hypotetraploid modes with chromosome numbers varying from 39 to 90, and acentric fragments and extra chromosomes appeared in 25-80% of the cells. This study of tumor cell cultures from *in vivo* carcinogen-induced tumors indicates that *in vitro* chemical transformation is a relevant model system for carcinogenesis since the characteristics of the tumor cell lines in culture paralleled for the most part the observations seen with *in vitro* transformation by this same class of carcinogens.

332 CARCINOGENIC EFFECTS OF POLYCYCLIC HYDROCARBON CARCINOGEN ADMINISTRATION TO MICE DURING PREGNANCY ON THE PROGENY. (E) Gulay, O. M. (Dept. Path., Ankara U., Turkey) and W. Wattenberg. *J Nat Cancer Inst* 46(2):397-402, 1971.

On days 11, 13 and 15 of pregnancy, female ICR/Ha mice were given i.p. injections of benzo(a)pyrene (BP, 4 mg) or 7,12-dimethylbenz(a)anthracene (DMBA, 2 or 4 mg). The progeny at birth were either nursed by foster mothers or by their own mothers, and tumor development was observed. Maternal exposure to BP was found to result in an increase in pulmonary adenomas among offspring nursing on their own mothers; progeny of mothers given BP showed a tumor incidence 35% greater than that of progeny of mothers not given BP. Progeny of mothers given

BP and delivered by caesarian section which were nursed by foster mothers also had a higher incidence of pulmonary adenomas than progeny of caesarian-delivered, non-nursing mothers not given BP; the former group developed 65% more tumors than the latter. DMBA was found to be a more potent inducer of pulmonary adenomas among offspring of treated mothers than BP. Progeny of BP-treated mothers delivered by caesarian section and nursed by foster mothers developed fewer tumors (39.5%) than progeny of DMBA-treated, caesarian-delivered, non-nursing mothers (48.0-97.7%), the percentage increasing with increasing dosage of DMBA. Both BP and DMBA, when given to mothers, increased the incidence of skin papillomas induced by topical application of croton oil in the progeny. DMBA given to mothers induced ovarian tumors in the female progeny of treated mice; however, BP had no such effect.

1333 3,4-BENZOPYRENE CONTENT IN HUMAN ORGANS OF VARIOUS AGE GROUPS. (Ger.) Graf, W. (Inst. Hyg., U. Erlangen-Nürnberg, Germany). *Arch Hyg Bakt* 154(4):331-335, 1970.

The benzo(a)pyrene (BP) content in various organs of man was analyzed and the findings were classified according to age; liver, spleen, kidneys, cardiac and skeletal muscle BP contents were divided into 6 groups according to age: 0 to 1 yr; 1 to 5; 5 to 15; 15 to 25; 25 to 50; and over 50 yr. The results revealed 2 maximal BP concentrations in each of the organs investigated; these maxima occurred in infancy and again in the age group over 50 yr. A V-shaped curve emerged when the mean values of the total BP contents were plotted according to age, again showing peaks at infancy and old age, with a minimum in the age bracket between 5 and 15 yr. In all age groups the highest mean values of BP were found in skeletal musculature and in the kidneys, and the mean value in BP content of all the organs investigated was 0.32 µg/100 gm dry wt. The presence of the carcinogen in the infant may be ascribable to endogenous sources, but the concentration in the higher age groups is consistent with exogenous and cumulative action.

1334 STIMULATORY EFFECT OF BENZO(a)PYRENE AND PHENOBARBITAL PRETREATMENT ON THE BILIARY EXCRETION OF BENZO(a)PYRENE METABOLITES IN THE RAT. (E.) Schlede, E. (Pharmacol. Inst. Free U. Berlin, Germany), R. Kuntzman and A. H. Conney. *Cancer Res* 30(12):8298-2904, 1970.

Female rats were treated daily with 20 mg/kg of benzo(a)pyrene (BP) p.o. or with i.p. injections of 37 mg/kg of phenobarbital; treatment periods for BP and phenobarbital were 2 and 4 days, resp. Twenty-four hr after pretreatment, rats were given i.v. injections of 10 or 300 µg ¹⁴C-BP. The concentration of radioactive BP metabolites in the bile 7 min after injection of 300 µg of labeled BP was 20-fold higher than in the controls given no pretreatment; after injection of 10 µg of labeled BP, the concentrations of metabolites was 6-fold higher in pretreated than in control rats. By 300-420 min after injection, BP metabolites in the bile of pretreated and control

rats given 10 µg labeled BP had declined to 9 and 12 dpm/µl bile, resp.; initial values for BP metabolites in the bile of pretreated and control rats were, resp., 300 and 50 dpm. Pretreatment with phenobarbital also enhanced ¹⁴C-BP metabolite concentrations in bile. Pretreatment of rats with ¹⁴C-labeled metabolites of BP had no effect on concentrations of BP metabolites in bile, which appeared to indicate that pretreatment with BP or phenobarbital did not enhance the transport of BP metabolites into bile, but enhanced the formation of BP metabolites. Evidently, the hydroxylation of ¹⁴C-BP in living rats is potentiated by pretreatment with BP, while phenobarbital does not produce this effect. Pretreatment with phenobarbital may enhance the biliary excretion of labeled BP metabolites by enhancing the conjugation of hydroxylated BP metabolites.

- 1335 EFFECT OF ENZYME INDUCTION ON THE METABOLISM AND TISSUE DISTRIBUTION OF BENZO(a)PYRENE. (E.) Schlede, E. (Pharmacol. Inst. Free U. Berlin, Germany), R. Kuntzman, S. Haber and A. H. Conney. *Cancer Res* 30(12):2893-2897, 1970.

The effect of pretreatment with benzo(a)pyrene (BP), 3-methylcholanthrene (MC) or 7,12-dimethylbenz(a)anthracene (DMBA) on the metabolism of BP was investigated in rats. Rats were given p.o. doses of 1 of the hydrocarbons once daily for 2 days prior to the i.v. administration of 115-250 µC of ³H-BP, and the disappearance of the labeled compound from blood, liver, brain and fat was examined. BP content in the blood of untreated controls and pretreated rats in the first min following the injection of ³H-BP was 193 and 155 ng/ml, resp. By 5 min postinjection, ³H-BP in the blood of controls was 30 ng/ml of blood, while in the rats pretreated with nonradioactive BP, the level was 5 ng/ml. Levels of ³H-BP in pretreated animals were consistently below those in controls. In the blood of rats pretreated with MC the ³H-BP level was 0.5 ng/ml, while in the blood of controls ³H-BP levels were 2.9, and DMBA pretreatment reduced ³H-BP concentrations to 0.7 ng/ml. Phenobarbital pretreatment reduced ³H-BP levels to 2.3 ng/ml compared to 2.5 ng/ml for controls. As with phenobarbital, pretreatment with anthracene or pyrene did not affect disappearance of ³H-BP. After 7 administrations of tritiated BP the ³H-BP content of rat fat was lower than after a single dose of the labeled compound, indicating that BP stimulates its own metabolism when administered chronically.

- 1336 THE STUDY ON THE MALIGNANT CHANGES OF BRONCHIAL EPITHELIAL CELLS IN MICE INDUCED BY THE INHALATION OF PARA-BENZOQUINONE. (Jap.) Otsu, H. (Sch. Med. Chiba U., Japan). *J Chiba Med Soc* 46(4):461-472, 1970.

Forty-five mice were maintained for more than 300 days on a regimen of para-benzoquinone inhalation (200 mg/day in a 340 l chamber); 4 mice developed lung cancer, 7 developed atypical adenomatous proliferation and 5 developed atypical growths of the terminal bronchial cells. Cancer cells showed stronger color development associated with cathepsin activity than

did terminal bronchial epithelial cells or atypical adenomatous proliferative cells. The color development was strongest in the area corresponding to the clear portion of the cytoplasm in the cancer cells. Under the light microscope, some cancer cells showed clear vacuolar areas of cytoplasm adjacent to the stroma; these areas stained only weakly with eosin, but had intact nuclei. Under the electron microscope, cancer cells and atypical adenomatous proliferative cells showed little electron density in their cytoplasm near the stroma. These cells occasionally were seen to protrude a part of their cytoplasm through the basement membrane into adjoining stroma which then degenerated and became necrotic. These morphological changes were thought to be associated with invasion by malignant cells.

- 1337 EFFECT OF ADMINISTRATION OF 3-METHYLCHOLANTHRENE ON THE SALT-EXTRACTABLE CHROMATIN PROTEINS OF RAT LIVER. (E.) Yee, M. (Baylor Coll. Med., Houston, Tex.) and E. Bresnick. *Molec Pharmacol* 7(2):191-198, 1971.

Treatment with 3-methylcholanthrene (3-MC) (20 mg/kg body wt, i.p.) increased the efficacy of rat liver chromatin as a template for RNA synthesis; when the 3-MC chromatin system was extracted with 2 M NaCl chromatin RNA template activity returned to normal levels. The salt-extractable protein components of 3-MC-treated rat liver chromatin were investigated observing the incorporation of ¹⁴C-labeled lysine into NaCl extractable proteins. Twenty min after the administration of ¹⁴C-lysine to rats, the ratio of incorporation of the label in salt-extractable proteins in 3-MC-treated rats to that in controls was 1:3, while 30 min after treatment with the label this ratio was 1:9; 60 min after treatment, the ratio was 2:4. Although the enhanced incorporation of ¹⁴C-lysine into salt-extractable liver chromatin proteins was considerable by 3 hr after 3-MC treatment, maximum enhancement occurred between 6-24 hr after treatment with the carcinogen, at which time the specific activity of the salt-extractable protein fraction from the livers of drug-treated rats was twice the value observed in animals not given 3-MC. Treatment with 3-MC did not affect the incorporation of ¹⁴C-labeled tryptophan into the 2 M NaCl-extractable liver proteins.

- 1338 INTERACTION OF 3-METHYLCHOLANTHRENE WITH LECITHIN-CHOLESTEROL MIXED FILMS. (E.) Weiner, N. D. (Coll. Pharm. Sci., Columbia U., New York, N. Y.), I. Chawdry and A. Felmeister. *J Pharm Sci* 60(3):425-428, 1971.

When a 50:50 molar ratio mixed film of cholesterol and methylcholanthrene (MC) was spread, the film exceeded that formed by cholesterol, indicating that MC interacted with cholesterol. No discernible interaction was seen between MC and lecithin in films containing both as components. In films composed of cholesterol and lecithin in 50:50 ratios, the interaction of the film with MC was weak, suggesting that when the lipid-lipid interaction is maximal, MC-lipid interaction is minimal. The findings

appeared to indicate that the extent of MC-cholesterol interaction is influenced by the competitive interaction of cholesterol and lecithin. Such competitive interactions may explain the fact that lecithin and other phospholipids retard, while cholesterol enhances, the formation of tumors induced by MC and other hydrocarbons.

- 339 EFFECT OF COBALT CHLORIDE AND SODIUM COBALTINITRIDE ON THE GROWTH OF ESTABLISHED EPITHELIAL TUMORS INDUCED BY METHYLCHOLANTHRENE. (E.) O'Hara, G. P. (Sch. Pharm. Temple U., Philadelphia, Pa.), D. E. Mann, Jr. and R. F. Gautieri. *Pharm Sci* 60(3):473-474, 1971.

The effect of cobalt chloride and sodium cobaltinitrite treatment on the growth of established skin tumors in mice was investigated. Mice of both sexes were given minimal carcinogenic doses of methylcholanthrene (21 biweekly applications of minimal carcinogenic doses of methylcholanthrene in acetone). After the cessation of methylcholanthrene treatment, mice in 1 group were given 25 mg/kg cobaltous chloride, and mice in 2 other groups were given 50 or 60 mg/kg sodium cobaltinitrite (i.p. biweekly for 1 wk). It was found that the group of mice given 0 mg cobalt nitrite had twice as many tumor regressions and less than half the number of new tumors than controls receiving no cobalt, but this finding did not represent a significant change. There was no apparent difference between controls and cobalt-treated mice on tumor growth; cobalt treatment does not seem to affect the growth of established, differentiated tumors.

- 340 CHROMOSOMES OF MAMMARY CARCINOMAS INDUCED BY 3-METHYLCHOLANTHRENE IN RATS. (E.) Rajumdar, S. K. (Dept. Biol., Lafayette Coll. Easton, Pa.) and E. D. Rees. *J Heredity* 61(6):231-236, 1970.

Cytotype studies were performed on cells from mammary carcinomas induced in female rats by intrastatic administrations of 3-methylcholanthrene (40 mg/100 g body wt for 5 doses). The modal chromosome number for each of the tumors was the usual rat diploid number of 42. Chromosomes were studied in direct cell preparations, and in cells from short-term cultures. In short-term cell cultures, chromatid breaks, gaps, fragments, stickiness and heteromorphic chromosomes were seen in 20% of the carcinoma cells. Alterations for the most part involved the X, 4-10, number 11-13 and number 14-20 chromosome groups. Cytotypes were generally normal; marker chromosomes were rarely seen. Twenty-seven percent of diploid chromosomes in the short-term cell culture preparations lacked at least one number 11-13 group chromosome, possibly due to the loss of short chromosome arms.

- 341 THE BINDING OF 3-METHYLCHOLANTHRENE TO MACROMOLECULAR COMPONENTS OF RAT LIVER PREPARATIONS. (E.) Hey-Ferguson, A. (Baylor Coll. ed., Houston, Tex.) and E. Bresnick. *Molec Pharmacol* 72(2):183-190, 1971.

Rat liver homogenates were centrifuged for the separation of the 9000 x g supernatant fractions, and the binding of this fraction with 0.25 μ C 14 C-3-methylcholanthrene (3-MC) together with a pyridine nucleotide was studied. This mixture was examined by chromatographing the 100,000 x g supernatant liquid obtained by centrifugation of the incubation medium on Sephadex G-100. The elution pattern consisted of 2 UV-absorbing, radio-actively labeled peaks designated A and B; peak A was eluted in the void volume, and was thought to consist mostly of RNA, while peak B was partially excluded and consisted mostly of proteins. If microsomes or the pyridine nucleotide were deleted from the reaction mixture, peak B failed to appear on chromatography. Peak A appeared even in the absence of the pyridine nucleotide and microsomes. Treatment of rats with 3-MC 24 hr before death enhanced the height of peak B but did not markedly affect the formation of peak A. An elution peak analogous to peak A was found when the same procedures were carried out using rat heart and kidney homogenates; spleen homogenates did not give a peak A. Peak B was not formed in heart and spleen and was very low in kidney. The results seemed to confirm that 3-MC or a derivative of it binds to the macromolecular components of the 9000 x g supernatant fraction of rat liver homogenate; the function of the bound 3-MC remains speculative.

- 1342 THE MORPHOLOGICAL AND HISTOENZYMATIC PROPERTIES OF EXPERIMENTAL BRAIN SARCOMAS CULTURED *IN VITRO*. (E.) Renkawek, K. (Polish Acad. Sci., Warsaw) and H. Kroh. *Z Krebsforsch* 75(2):123-132, 1971.

The morphological and histoenzymatic properties of 15 experimental brain fibrosarcomas and giant cell sarcomas induced in C₃H strain mice by methylcholanthrene implantation were investigated in tissue culture. The fibrosarcoma from intra- and extra-cerebral tumors showed similar morphological features exhibiting slow growth with the first cells appearing after 1 wk; considerable cellular polymorphism with a relatively monotypic appearance of the nuclei was observed. In cultures of tumors identified in tissue sections as giant cell sarcomas, the tumor cells grew out of the explant on the third day of culture and exhibited expansive growth with highly polymorphic nuclei containing distinct granular chromatin and numerous atypical mitoses. The amount of PAS-positive granules was less in the giant cell sarcoma whereas the fibrosarcoma cells showed high glucose-6-phosphate dehydrogenase activity. These findings agreed with results previously reported by other investigators.

- 1343 THE ACTIVITY OF COLLAGENASES AND COLLAGEN CONTENT IN THE SKIN DURING CARCINOGENESIS. (Ger.) Rohrbach, R. (Path. Ins. U. Freiburg, Germany), C. Thomas, R. Rümpler and M. Lau. *Verhandl Deutsch Ges Path* 54:442-450, 1970.

Collagenolytic activity was investigated in hairless mice during carcinogenesis of the skin induced by methylcholanthrene and dimethylbenzanthrene solutions

in acetone (0.25%). The mice were sacrificed at different times, and the epidermis with the corium and papillomas or carcinomas were examined after suitable preparation. The DNA content/dry wt of corium and epidermis remained unaltered in the acetone-treated controls, and the epidermis of these animals showed a two-fold higher DNA content than the corium. In the experimental animals the DNA content of the epidermis was decidedly increased and that of the corium only slightly increased. The DNA content of the skin papillomas was 50-70% higher than that of the tumor-free surrounding tissue. Collagenase activity in the carcinogen-treated skin was markedly higher in the corium than in the epidermis. The DNA content of the benign skin papillomas and of peripheral carcinoma portions was about the same, but the carcinoma periphery showed a higher collagenase activity. The application of carcinogens for 20 wk produced a 50% increase in DNA content and a 300% increase in collagenolytic activity, which was particularly marked in the corium. Although a decided difference in collagen activity is shown between neoplastic and healthy skin, the changes may not be applicable to internal organs.

- 1344 PROPERTIES OF CYTOCHROME P-450 AS AFFECTED BY ENVIRONMENTAL FACTORS: QUALITATIVE CHANGES DUE TO ADMINISTRATION OF POLYCYCLIC HYDROCARBONS. (E.) Mannering, G. J. (U. Minnesota Coll. Med. Sci., Minneapolis). *Metabolism* 20(2):228-245, 1971.

The effect of polycyclic hydrocarbons on the properties of cytochrome P-450 was studied in rat hepatic microsomes through metabolic and spectrophotometric techniques. N-demethylation of ethylmorphine was inhibited 35-47% in non-pretreated controls, phenobarbital- and 3-methylcholanthrene-treated rats with administration of 2-diethylaminoethyl-2,3-diphenylvalerate hydrochloride; N-demethylation of 3-methyl-4-methylaminoazobenzene was also inhibited. However, in the 3-methylcholanthrene-treated rats 10 times more reagent was needed to exert a 50% inhibition. Spectral peaks observed at 430 and 455 nm were plotted against pH independently to give an intercept at about pH 7.4 for untreated and phenobarbital-treated animals; for 3-methylcholanthrene-treated animals, the intercept was at pH 6.9, indicating the formation of a new hemoprotein P₁-450. The second peak seen with microsomes from animals treated with polycyclic hydrocarbons was located at 453 nm rather than at 455 nm. The pH intercept was shown to bear an inverse relationship to the increased rate of N-demethylation. Aggregated cytochrome P₁-420 showed type II binding only upon desalting in contrast to type I and II binding with drugs seen with cytochrome P-420; absolute spectra of cytochrome P₁-450 differed only slightly from those produced by cytochrome P-450, and incubation of microsomes with polycyclic hydrocarbons did not cause the formation of a P-450 hemoprotein with characteristics of cytochrome P₁-450. That cytochrome P₁-450 may be an aberrant hemoprotein is suggested by its absence in measurable quantity in microsomes from untreated rats and by its apparent lack of a type I binding site.

- 1345 DIETHYLNITROSAMINE CARCINOGENESIS. (E.) Mohr, U. (Med. Coll. Hannover, Germany). *Fortschr Med* 89(6):251-253, 1971.

Experimental pulmonary tumors were obtained in the golden hamster with diethylnitrosamine (DENA) administered by p.o. intubation, intratracheally spray, or s.c. injection. Basal cell hyperplasia and squamous epithelial metaplasias were obtained in the area of the mucosa of the tracheobronchial tree within a few wk, and after 4 months of treatment longer, tracheal papillomas developed as well as squamous epithelial and adenocarcinomas of the lung. The s.c. administration produced tumors in the shortest period of time. The concept of organotropy supported by this type of experiment, since in the p.o. intubation of DENA produced neoplasms in the liver and kidneys. Other experiments in the golden hamster with nitrosamine derivatives, acetoaminofluorene and benzopyrene also led to pulmonary tumors. The carcinogen (DENA) was also tested in pregnant animals by s.c. injections during the second half of their pregnancy. After 25 wk, 74% of the mothers and 42% of the offspring showed the squamous epithelial metaplasias in the respiratory mucosa.

- 1346 DIMETHYLNITROSAMINE FORMATION FROM SODIUM NITRITE AND DIMETHYLAMINE BY BACTERIAL FLORA OF RAT INTESTINE. (E.) Klubes, P. (George Washington U. Sch. Med., Washington, D. C.) and W. R. Jondro. *Res Commun Chem Path Pharmacol* 2(1):24-34, 1971.

The formation of the carcinogenic compound dimethylnitrosamine from dimethylamine and sodium nitrite by bacterial flora in the rat cecal contents was investigated. Rat cecal contents were incubated with ¹⁴C-labeled dimethylamine and sodium nitrite at neutral pH under anaerobic conditions, resulting in synthesis of 70-108 μmoles of nitrosamine in the presence of 20 hr. The omission of glucose from the reaction system diminished the yield of dimethylnitrosamine, suggesting that the formation of the carcinogen is dependent on the metabolic activity of the intestinal microorganisms. Inasmuch as nitrites are common additives, these results suggest that dimethylnitrosamine synthesis from dimethylamine in the presence of nitrites constitutes a risk for humans.

- 1347 CARCINOMA OF THE GALLBLADDER INDUCED IN HAMSTERS BY INSERTION OF CHOLESTEROL CRYSTALS AND FEEDING DIMETHYLNITROSAMINE. (E.) Kowalewski, K. (Surg. Med. Res. Inst., U. Alberta, Edmonton, Canada) and E. F. Todd. *Proc Soc Exp Biol Med* 136(2):482-486, 1971.

The induction of gallbladder neoplastic lesions resulting from chronic, nonspecific irritation of the gallbladder mucosa induced by an "experimental cholesterol gallbladder stone" was studied in dimethylnitrosamine-treated male hamsters. In dimethylnitrosamine-treated animals hepatocellular and cholangiocarcinomas resulted in which proliferating bile ducts were lined with atypical epithelial cells showing abnormalities in nuclear polarity, variation in nu-

size and shape, hyperchromatism and an increase in the number of mitotic figures. Sixty-eight percent of dimethylnitrosamine-treated animals with implanted cholesterol pellets developed carcinoma of the gallbladder and only 1 animal without pellet implantation showed signs of carcinoma of the gallbladder. Gallbladder pellets alone had no carcinogen effect even after 40 wk of implantation. Experimental gallbladder stones appear to enhance the malignant transformation of gallbladder mucosa in dimethylnitrosamine-treated animals, but diethylnitrosamine did not affect the gallbladder.

- 1348 DIFFERENCES IN TUMOR TYPES AND ORGAN SUSCEPTIBILITY IN BALB/c AND RF MICE FOLLOWING DIMETHYLNITROSAMINE AND DIETHYLNITROSAMINE. (E.) Clapp, N. K. (Oak Ridge Natl. Lab., Tenn.), R. L. Tyndall and J. A. Otten. *Cancer Res* 31(2):196-198, 1971.

The oncogenic effects of dimethylnitrosamine (DMN) and diethylnitrosamine (DEN) in adult BALB/c mice were compared to previously reported effects on RF/Un mice; the carcinogens were administered in drinking water for varied periods of time. Liver hemangiosarcomas were induced by both carcinogens in BALB/c mice and by dimethylnitrosamine in RF/Un mice, while diethylnitrosamine induced liver hepatomas in RF mice and forestomach and esophageal squamous cell carcinomas in both strains. In addition, dimethylnitrosamine treatment resulted in lung adenomas in both strains. The data suggest that the strain susceptibility to tumor induction is not necessarily related directly to the carcinogenic results following treatment with a powerful carcinogen; however, a compound-enzyme specificity may exist within certain cells of an organ which enables these cells to metabolize the carcinogen to a proximate carcinogen.

- 1349 CHANGES IN THE CONCENTRATIONS OF NUCLEIC ACIDS AND HISTONE IN EXPERIMENTALLY INDUCED TUMORS: CYTOPHOTOMETRIC STUDIES. (Ger.) Tasca, C. (German Cancer Res. Ctr., Heidelberg), D. Haag and K. Goerttler. *Verhandl Deutsch Ges Path* 54:458-464, 1970.

An account of small but definite deviations from the norm in 10 experimentally produced tracheal papillomas is presented. The tissues were obtained from pregnant golden hamsters which had been injected with 50 mg/kg of diethylnitrosamine and from their offspring. The morphological changes investigated were nuclear volumes, nucleic acid content, and the histone content compared with normal tracheal mucosa. Nuclear volumes of the papilloma cells were twice that of normal mucosa cells, and a corresponding decrease was seen in concentration of DNA, total nucleic acids, and histones in the papillomas compared with normal tissue and the total amount of DNA, total nucleic acids, and histones were only slightly increased over normal cells. Correlations between DNA and total nucleic acid quantities and nuclear cell volume were obtained by means of regression analysis, which showed that there was a disturbance in these ratios

in the papilloma cells. Although there was no sharp change between the normal and diseased cells by this method, there appeared to be a continuous transformation which was detected by mathematical calculations. (13 references)

- 1350 SPECIFIC PHASES OF GROWTH-BEHAVIOR OF PRENEOPLASTIC CELLS DURING CARCINOGENESIS. (Ger.) Rabes, H. (Path. Inst. U. Munich, Germany), P. Scholze and R. Hartenstein. *Verhandl Deutsch Ges Path* 54:428-433, 1970.

The rate of cell proliferation during diethylnitrosamine (DENA) carcinogenesis was followed in the livers of partially hepatectomized and intact rats by monitoring ^3H -thymidine incorporation. From the start of DENA feeding (5 mg/kg daily) up until 130 days, 2 rats were injected with the ^3H -thymidine every 10 days, and 3 rats were partially hepatectomized every 10 days and injected with ^3H -thymidine 20 to 56 hr after hepatectomy. The liver was removed 4 hr after the last injection, and histochemical studies were made on cryostat serial sections. Changes in the growth fraction were observed 10 days after DENA feeding in the partially hepatectomized animals, and enzymatic activity and DNA synthesis were inhibited. The enzyme depleted liver cells showed only a slight proliferation on the 90th day, but proliferation was abundant in partially hepatectomized animals. At about the 120-130th days there was a marked increase in proliferation. A latent period of variable intervals occurred in tumor formation, which was dependent upon the homeostatic regulation of the specific organ.

- 1351 DIBUTYLNITROSAMINE CARCINOGENESIS IN SYRIAN GOLDEN AND CHINESE HAMSTERS. (E.) Althoff, J. (U. Nebraska Coll. Med., Omaha), F. W. Krüger, U. Mohr and D. Schmahl. *Proc Soc Exp Biol Med* 136(1):168-173, 1971.

The carcinogenic effects of dibutylnitrosamine (DBN) were investigated in male Syrian golden hamsters and Chinese hamsters. Hamsters were given intragastric or s.c. injections of 300 mg/kg body wt of DBN once a wk for life. Intragastric and s.c. injection produced similar mortality and carcinogenic effects. By 23 wk after the treatment was begun papillomas were found in the urinary bladders of hamsters; squamous cell carcinoma areas were also seen. In the nasal and paranasal cavities of both Syrian and Chinese hamsters, papillomas were observed after 30 wk and squamous cell carcinomas after 35 wk. Tumor incidences approached 5-10%. Tracheal papillomas developed in Syrian hamsters by wk 23, and lung tumors developed after wk 25. In Syrian hamsters, lesions of the upper digestive tract were rare; however, in Chinese hamsters, 25% of the animals developed papillomas or squamous cell carcinomas on the hard palate or elsewhere in the oral cavity. Multiple papillomas in the forestomach were also common.

- 1352 MORPHOGENESIS AND FINE STRUCTURE OF EXPERIMENTAL RENAL CLEAR CELL TUMORS. (Ger.) Bannasch, P. (Path. Inst. U. Würzburg, Germany) and

U. Schacht. *Verhandl Deutsch Ges Path* 54:464-471, 1970.

Clear cell adenomas and carcinomas induced by N-nitrosomorpholine administered to rats in their drinking water in the concentration of 12mg% are described. Out of the 97 experimental animals with various types of epithelial renal tumors, 18 developed predominantly or partially clear cell tumors 4-19 months following the administration of the carcinogen. Morphologically these tumors resembled those described in humans by Grawitz and were so small that most could only be perceived microscopically, but some could grow to a diameter of about 2 cm. The light microscopic and electron microscopic studies showed the characteristic glycogen masses in layers of cytoplasm, and, more rarely, lipid deposits, a few mitochondria, and single ergastoplasm profiles and free ribosomes. Some of the tumor cells contained an abundance of mitochondria with many morphological changes. It was also possible to follow the cell transformation in the renal tubules, the formation into cyst-like shapes and further development into transparent epithelium. The glycogen storage cells in the first stages of tumor formation were transformed into glycogen-free tumor cells and eventually resulted in a glycogen-free tumor.

1353 ESTABLISHMENT OF FOUR LINES OF TRANSPLANTABLE RAT LEUKEMIA INDUCED BY N-NITROSOBUTYLUREA IN DONRYU RATS. (E.) Odashima, S. (Nat'l. Inst. Hyg. Sci., Tokyo, Japan) and F. C. Wang. *Gann* 61(6):597-600, 1970.

Establishment of 4 lines of myelogenous leukemia in Donryu rats induced by N-nitrosobutylurea (0.01% in drinking water till sacrifice) and application of various carcinogens (4-nitroquinoline-1-oxide, N-nitrosobutylurea, N-methyl-N'-nitro-N-nitrosoguanidine or 7,12-dimethylbenz(a)anthracene) to the mucosal surface of the glandular stomach has been studied. Smear preparations of ascites and peripheral blood of test animals following i.p. injection of 1-2 ml of blood from leukemic rats revealed leukemic cells in 1-wk-old ascites in 8 of 10 cases, but they were not detected in 3-wk-old ascites except 1 in which tumor cells grew progressively until death. One to two-wk-old tumor ascites transferred i.p. into the second generation showed 4 of 7 lines growing successfully. In one line (DBLA-10), the median survival time was 85 days compared to a 14-20 day period for the remaining 3 lines (DBLA 1, 6 and 9). In these 3 lines, leukemic cells proliferated rapidly reaching a pure culture state in 7-10 days followed by rapid degeneration of leukemic cells whereas the DBLA-10 line proliferated gradually and reached a pure culture state in several wk after inoculation. In lines 1, 6 and 9 an increase in WBC was seen 5-7 days after inoculation and continued to increase even after disappearance of leukemic cells from the ascites. In line 10 WBC did not increase in most cases and only a few leukemic cells were detectable in the circulating blood. Autopsy findings in lines 1, 6, and 9 showed proliferation of leukemic cells in spleen, periportal tissues of the liver and its sinusoids, thymus and bone marrow, interstitial tissues

of the kidney, adipose tissue of the peritoneal cavity, lung alveoli and lymph nodes, whereas in line abundant tumor nodules appeared on the peritoneal surface accompanied by enlargement of thymus and hepatosplenomegaly.

1354 LEIOMYOSARCOMAS INDUCED BY ORAL ADMINISTRATION OF N-METHYL-N'-NITRO-N-NITROSOGUANIDINE IN GASTRIC CYSTS GRAFTED IN SUBCUTANEOUS TISSUE OF MICE. (E.) Matsuyama, M. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan), H. Suzuki and T. Nakamura. *Gann* 61(6):523-527, 1970.

The carcinogenic effects of N-methyl-N'-nitro-N-nitrosoguanidine (NG) on gastric cysts developed on stomach grafts were investigated in mice. New-born mice of both sexes were engrafted with sheets of the glandular stomach of litter mates. At 2 months of age when the gastric cysts were established in the s.c. tissue, the mice were started on continuous administration of NG in their drinking water (50 mg/L). All the cysts of mice given NG contained chocolate-colored, condensed solution, while cysts of mice given water were clear and serous. Leiomyosarcomas developed in the grafts in 5 of 20 NG-treated mice, and atypical hyperplasia developed in the cyst epithelial cells in 2 cases; no tumors developed in control animals. The latency period for formation of tumors on the grafts was 311-415 days. Lung adenomas and ovarian tumors were also found in the NG-treated mice. The mechanism by which NG causes tumorigenesis in the cysts is obscure.

1355 PROMOTION BY DNA OF THE PHOTOINDUCED RADICAL PRODUCTION FROM 4-NITROQUINOLINE-1-OXIDE IN AQUEOUS MEDIUM AT 77°K AND ITS MECHANISM (E.) Okano, T. (Tohoku U. Sch. Med., Sendai, Japan), A. Takadate and K. Uekama. *Gann* 61(6):541-549, 1970.

Quantitative examinations on the electron spin resonance spectroscopic behavior of 4-nitroquinoline-1-oxide in the presence of DNA and its nucleosides were made utilizing calf-thymus DNA, deoxyguanosine, deoxyadenosine, deoxythymidine and deoxycytidine. The electron spin resonance spectra exhibited a weak signal at 77°K which was seen to become larger as the time of photoirradiation progressed; no signal was observed at room temperature irrespective of photoirradiation. The second derivative exhibited a single peak after 20 min of photoirradiation, and the presence of DNA did not promote any signal with or without photoirradiation, and the g-value (2.006) and line widths (21 gauss) of the original spectrum were unaffected. The 4 component nucleosides exhibited no signal, and the extent of the promotive effect on radical production decreased in the order of deoxyguanosine>deoxyadenosine>deoxythymidine>deoxycytidine.

1356 DNA REPAIR SYNTHESIS IN MAMMALIAN CELLS EXPOSED TO A SERIES OF ONCOGENIC AND NON-ONCOGENIC DERIVATIVES OF 4-NITROQUINOLINE-1-OXIDE (E.) Stich, H. F. (Cancer Res. Ctr., U. British Columbia, Vancouver, Canada), R. H. C. Smith and Y. Kawazoe. *Nature* 229(5284):416-419, 1971.

Unscheduled DNA synthesis was observed by autoradiographic studies of the incorporation of ^3H -thymidine into cultured Syrian hamster cells exposed to various isomeric and substituted 4-nitroquinoline-1-oxides. Among the various isomeric nitroquinoline-1-oxides, only the highly oncogenic 4-nitroquinoline-1-oxide-induced lesions resulted in extensive DNA repair synthesis, while virtually all substituted derivatives elicited DNA repair synthesis in varying dose-dependent degrees; maximal levels of label incorporation occurring in cells exposed to weakly oncogenic derivatives were lower than in tissues treated with highly oncogenic compounds. The hydroxyamino acid and pyridine derivatives elicited relatively high DNA repair synthesis. Initial treatment with ultraviolet irradiation produced no remarkable change in DNA synthesis, but an additive effect was noted when applications of two carcinogens were used at intervals of less than 10 hr. Compounds active in eliciting DNA repair synthesis exerted an inhibitory effect on the entry of cells into the S phase while cells exposed to 4-nitroquinoline-1-oxide before addition of oncogenic SA7 virus resulted in at least a 20-fold increase in transformation frequency from cells infected with the virus alone.

- 1357 CYTOCIDAL ACTION OF CARCINOGENIC 4-NITROQUINOLINE-1-OXIDE AND RELATED COMPOUNDS. (E.) Tokuzen, R. (Natl. Cancer Ctr. Res. Inst., Tokyo, Japan), M. Araki, M. Saneyoshi and F. Fukuoka. *Gann* 61(6):601-603, 1970.

The cytotoxic activity of carcinogenic 4-nitroquinoline-1-oxide and related compounds was assayed by incubating Nakahara-Fukuoka sarcoma grafts with 0.05-0.005% of the test compound for 24 hr and then observing the growth of the tumor after transplantation into mice. The cytotoxic and carcinogenic activity of the parent nitroquinoline compounds and their corresponding hydroxyamino-derivatives paralleled each other completely. The relationship between the cytotoxic and carcinogenic actions of this group was further supported by the absence of cytotoxic activity in the non-carcinogenic quinoline derivatives such as 4-aminoquinoline-1-oxide, 4-hydrazinoquinoline-1-oxide, 4-acetylhydrazinoquinoline-1-oxide, 4-azidoquinoline-1-oxide, 8-hydroxyquinoline-1-oxide, and 3-nitro-4-hydroxyquinoline-1-oxide.

- 1358 METABOLISM OF CARCINOGENIC 4-HYDROXYAMINOQUINOLINE-1-OXIDE IN MICE. (E.) Kawazoe, Y. (Natl. Cancer Ctr. Res. Inst., Tokyo, Japan), M. Tamura and M. Araki. *Gann* 61(6):593-596, 1970.

The metabolism of 4-hydroxyaminoquinoline-1-oxide in ddN strain female mice was studied by the reverse dilution method utilizing ^3H -labeled metabolites. The subcutaneously administered carcinogen (0.5 mg) was quickly metabolized even at the site of injection into 4-aminoquinoline-1-oxide, 4-aminoquinoline, and 4-hydroxyquinoline-1-oxide with maximum concentrations in blood appearing within 0.5 hr after the injection. At the earlier stages the main constituent extracted from all sites examined was 4-hydroxyamino-

quinoline-1-oxide; at injection site, blood and lung 4-hydroxyquinoline-1-oxide was the main component with the liver showing 4-aminoquinoline in highest concentration.

- 1359 DEVELOPMENT OF SARCOMAS IN MICE AT SITE OF INJECTION WITH A NEW CARCINOGEN, MONO-ACETYL DERIVATIVE OF 4-HYDROXYAMINOQUINOLINE. (E.) Sato, K. (Fac. Educ., Hirosaki U., Japan), T. Saito and M. Enomoto. *Jap J Exp Med* 40(6):475-478, 1970.

Female mice given 20 s.c. injections of 0.12 mg of a monoacetyl derivative of 4-hydroxyaminoquinoline (AcHAQ) developed fibrosarcomas and myosarcomas at the injection site in 17 of 20 DDD mice. A diacetyl derivative of 4-hydroxyaminoquinoline (DiAcHAQ, 0.15 mg) induced similar sarcomas in 13 of 21 mice. AcHAQ produced sarcomas in 84 days from the day of injection, while DiAcHAQ produced tumors in 102 days. AcHAQ also induced lung adenomas and s.c. sarcomas in 20 of 30 mice injected shortly after birth with 53 μM moles of the agent; 4-nitroquinoline-1-oxide (53 μM moles) induced tumors in 6 of 18 animals. The high carcinogenic activity of AcHAQ suggests that this compound might be a proximate carcinogen of 4-nitroquinoline.

- 1360 L-CYSTEINE AS PROTECTOR AGAINST ABERRATION RELEASING ACTION OF 8-HYDROXYQUINOLINE SULFATE IN HUMAN LEUKOCYTE CHROMOSOMES. (Ger.) Gebhart, E. (Inst. Humangenet., U. Erlangen-Nuremberg, Germany). *Mutat Res* 11(2):261-262, 1971.

The protective action of L-cysteine against 8-hydroxyquinoline sulfate (8-HCHS) was tested in human lymphocyte cultures from the peripheral blood of blood donors. The tests were conducted for different time intervals (24 hr, 1 hr) and with different concentrations of 8-HCHS (5.10^{-6}M , 1.10^{-5}M), for 100 metaphases. The cysteine effect reduced substantially the metaphases with chromosomal structure defects, especially the chromatid gaps and the isochromatid gaps. In addition, L-cysteine was shown to affect the last period of the S-phase (6 hr recovery), the aberrant metaphases dropping from 52% to 17% in the first case and from 37% to 24% in the second case. Treatment with L-cysteine after lymphocyte incubation with 8-HCHS revealed the protective effect of this substance to be even more marked, especially in the chromatid- and isochromatid gaps.

- 1361 TUMOR INDUCTION BY REPEATED INJECTIONS OF URETHAN IN NEWBORN AND ADULT HAMSTERS: AGE INFLUENCE. II. (E.) Toth, B. (U. Nebraska Coll. Med., Omaha). *J Nat Cancer Inst* 46(1):81-93, 1971.

The study of age influence in urethan-induced carcinogenesis in Syrian golden hamsters at birth and adult age is reported. Day-old and 8-week-old hamsters were given a single i.p. injection of urethan (1 mg/g body wt) once a wk for 9 wk. Nine of the females in which treatment was started at birth developed 16 tumors of the cecum, 8 of which were polypoid

adenomas and the remainder, adenocarcinomas. In newborn males, 13 developed 23 cecal tumors, 12 of which were classified as polypoid adenomas and 11 as adenocarcinomas. Seven females in which treatment was started at 8 wk developed 8 cecal tumors, 4 of which were classified as polypoid adenomas and the remainder as adenocarcinomas; 8 males developed 9 cecal tumors, 5 of these being polypoid adenomas, and 4 were adenocarcinomas. In males in which treatment was started at birth, 2 developed 2 adenomas of the colon at 82 and 112 wk, and 2 males had 3 adenocarcinomas at 50, 50 and 101 wk; 1 female developed an adenocarcinoma at 40 wk, and 1 female whose treatment started at adulthood developed a similar tumor at 87 wk. In animals in which treatments were started at birth, 8 females developed 8 thyroid tumors, 6 of which were adenomas of the thyroid and 2 were carcinomas; 3 males developed 2 adenomas and 1 carcinoma of the thyroid. With treatment started at 8 wk, 6 females developed 6 adenomas of the thyroid and 1 carcinoma, with a single adenoma observed in 1 male. Dermal melanocytomas occurred in 26 of 40 female and 21 of 33 male animals injected at birth, while 41 melanocytomas among 38 females and 27 among 39 males developed when injections started at 8 wk. Squamous cell carcinomas of the forestomach were seen in 2 animals of each sex in which treatments were started at birth and in 5 females and 4 males receiving first injections at 8 wk.

- 1362 *IN VIVO* INTERACTION OF URETHAN WITH NUCLEIC ACIDS AND PROTEINS. (E.) Prodi, G. (Inst. Gen. Path., U. Bologna, Italy), P. Rocchi and S. Grilli. *Cancer Res* 30(12):2887-2892, 1970.

In vivo studies on the interaction of urethan with nucleic acids and proteins of rat organs was followed with the use of labeled carbamate compounds. All fractions of the organs (liver, spleen, lung, kidney, skin) showed considerable radioactivity 24 hr after injection with ethyl carbamate- $1-^{14}\text{C}$ with protein fractions showing higher activity than that of nucleic acids; maximum binding was noted in skin, and in decreasing order, in spleen, lung, liver, and kidney. RNA activity was higher than DNA activity in all organs except that of kidney RNA which exceeded that of liver RNA. DNA activity versus time was almost constant and RNA activity increased from 15 to 48 hr, while nuclear protein activity peaked at 15 hr and cytoplasmic protein showed differences in various organs with the use of ethyl carbamate- $2-^3\text{H}$. Activity found in all organs 24 hr after i.p. injection of ethyl carbamate carboxyl- ^{14}C was 20- to 100-fold lower than that determined with ethyl carbamate- $1-^{14}\text{C}$. Acid hydrolysis of RNA removed radioactivity from AMP and GMP; characteristics of the labeled moiety was not coincidental with ribose, adenine, or guanine. DNA did not react to acid hydrolysis. Urethan interaction with nucleic acids appears not to be due to metabolic utilization of the labeled compound in the synthesis of nucleotides.

- 1363 INCIDENCE OF CANCER IN MEN ON A DIET HIGH IN POLYUNSATURATED FAT. (E.) Pearce, M. L. (Wadsworth Hosp. Med. Serv., VA Ctr., Los Angeles, Calif.) and S. Dayton. *Lancet* 1(7697):464-467, 1971.

The development of cancer in 846 men participating in a study of the effects of a high polyunsaturated fat diet on atherosclerotic events was investigated. Although atherosclerotic events were more common in the group maintained on a conventional diet, an excess of non-atherosclerotic deaths was observed in the experimental diet group. The excess was accounted for by a greater incidence of fatal carcinomas in the experimental group. In the conventional diet group, 17 deaths were due to carcinoma; in the polyunsaturated fat-rich diet group, there were 31 cancer deaths. There was a higher incidence of visceral carcinomas in the experimental group than in the control group. Cancers of the lung and bronchus were the most common malignancies in both experimental and control groups, accounting for 12 deaths in the control group and 16 deaths in the experimental group. Cigarette smoking habits were not correlated with carcinoma incidence in either group to the degree of statistical significance; no non-dietary explanation suggested itself for the frequency of cancer deaths in the experimental group.

- 1364 THE CYTOGENETIC EFFECT OF CYCLOPHOSPHAMIDE ON A BURKITT TUMOR CELL LINE (EB_4) *IN VITRO*. (E.) Bishun, N. P. (Marie Curie Mem. Found., Oxford, Surrey, England). *Mutat Res* 11(2):258-260, 1971.

Treatment of a cell culture from a Burkitt's lymphoma tumor arising in a 15-yr-old English girl with cyclophosphamide resulted in increased frequencies of chromosomal aberrations. Cells from the Burkitt tumor were arrested in metaphase by the addition of colchicine, and cyclophosphamide was added to cultures at amounts of 0.001, 0.01, 0.025 or 0.05 $\mu\text{g}/\text{ml}$. Cyclophosphamide treatment, in all 4 doses, increased occurrence of chromosomal aberrations, including polyploidy, chromatid breaks, chromatid gaps, quadriradials and rings. Chromosomal aberrations did not appear to be dose-related. In Burkitt's lymphoma cells treated with cyclophosphamide (0.001 μg), the percentage of polyploidy was 10.5, while in control cells the percentage was 1.5. Percentages of chromatid gaps and breaks in treated (0.01 μg) and untreated cells were 23 and 10, and 42 and 7, resp. Percentages of quadriradials in treated (0.025 μg) and untreated cells were 7 and 1, resp. Rings were seen only in control cells, and dicentric chromosomes were seen only in controls and in cells treated with (0.025-0.001 μg) cyclophosphamide.

- 1365 MYELOMONOCYTIC LEUKAEMIA SUPERVENING ON CHRONIC LYMPHOCYTIC LEUKAEMIA. (E.) Catovsky, D. (Roy. Postgrad. Med. Sch., London, England) and D. A. G. Galton. *Lancet* 1(7697):476-479, 1971.

A case is reported in which a 54-yr-old man developed myelomonocytic leukemia following remission of chronic lymphocytic leukemia. After approximately 6 yr of comparative good health following the disappearance of symptoms of chronic myelocytic leukemia, the patient presented with a lymphocyte count of 5000/ μ l, hypercellular bone marrow, and low serum-immunoglobulin levels. On the basis of lysozyme estimations, total vitamin B₁₂ binding capacity tests, and lymphocyte "blast" transformation studies, it was concluded that the patient had myelomonocytic leukemia. Chlorambucil, which the patient had received continuously for 40 months for treatment of chronic lymphocytic leukemia, may have been responsible for the subsequent development of myelomonocytic leukemia.

1366 EXPERIMENTAL STUDIES ON INTAKE AND DEPOSITION OF SMOKE PARTICLES IN GOLDEN HAMSTERS WHEN EXPOSED TO CIGARETTE SMOKE. (Ger.) Montenwill, W. (Res. Inst. Cigarette Industry, Hamburg, Germany), H. P. Harke, A. Baars and E. Goertz. *Arzneimittelforschung* 21(1):142-143, 1971.

The deposition of smoke particles in 10 male Syrian golden hamsters was investigated by means of n-hexadecane/n-hexadecane-1-¹⁴C. The animals were sacrificed immediately following their exposure to the smoke, and the lungs, trachea, larynx and tongue were analyzed for radioactivity. Radioactivity was determined in terms of labeled CO₂ derived from incineration of the respective organs. The results revealed that absorption in the nasal cavity was less than 50% of the smoke particles, and only about 20% of the activity was found in the head. In the respiratory tract, about 70% of the activity was found in the lungs, with 3-4% retained in the larynx, 3-6% on the tongue surfaces, and 1.5-3% in the trachea. The highest deposit of smoke particles per unit of surface was found in the area of the larynx.

1367 THE EFFECT OF CHRONIC INHALATION OF FRESH CIGARETTE SMOKE AND ITS GASEOUS PHASE UPON THE DEVELOPMENT OF PULMONARY TUMORS IN SNELL MICE. (Ger.) Leuchtenberger, C. (Swiss Inst. Exp. Cancer Res., Lausanne) and R. Leuchtenberger. *Z. Praeventivmed* 15(6):457-462, 1970

A smoking apparatus allowing for intermittent puffs of fresh air and fresh cigarette smoke was used to simulate human smoke inhalation in Snell mice. The type of pulmonary carcinoma found in man was not found in Snell mice but 2 types of glandular tumors were observed in these animals, benign adenomas and adenocarcinomas. The control male animals developed more spontaneous lung tumors (12.2%) than did the females (5.1%). Male mice exposed to whole cigarette smoke or to the gas phase only also had higher incidences of lung tumors (16.8% and 25.0%, resp.) than female mice (10.7% and 18.2%, resp.). Tumors developed after a shorter latent period in experimental animals than in controls, and animals exposed to the gas phase only had even shorter latent periods for tumor formation. These results indicate that the volatile components rather than the smoke particles are the active carcinogenic agents in tobacco smoke.

1368 ARSENIC AND EPITHELIOMAS OF THE SKIN. (Ger.) Fritsch, P. (U. Clin. Vienna, Austria), F. Schellander and K. Konrad. *Wien Klin Wschr* 83(1):7-11, 1971.

The role of arsenic as a carcinogen was studied by means of a questionnaire addressed to 619 subjects, of whom 419 had epitheliomas. The epitheliomas were comprised of deep and superficial basal cell carcinomas, Bowen's disease and Bowen carcinoma. The results of the questionnaire revealed that in the Bowen epithelioma and superficial basal cell carcinoma groups, positive histories of contact with arsenic were found in 36% of the cases compared with 14% of the controls. The type of exposure to arsenic was found to be due to medication more often than to exogenous contact, the latter being found more frequently in men than in women. More patients with epitheliomas reported contact with arsenic over a longer period of time than did the controls, and all the patients reported more numerous contacts with arsenic than did the controls. Bowen's disease and superficial basal cell carcinoma patients showed significantly more signs of chronic arsenic poisoning than did any of the other groups including controls. No definite conclusion could be drawn from these results to implicate arsenic as a carcinogen.

1369 LONG-TERM MORTALITY STUDY OF STEELWORKERS: V. RESPIRATORY CANCER IN COKE PLANT WORKERS. (E.) Lloyd, J. W. (Natl. Environ. Hlth. Sci., Natl. Inst. Hlth., Bethesda, Md.). *J. Occup Med* 13(2):53-68, 1971.

Investigation of statistics on mortality from all causes among steelworkers employed in 1953 and previously indicated that there is an excess of mortality from respiratory cancer among workers in the coke plant sector of steel plants; the observed respiratory cancer mortality among coke oven workers was 20, and the expected mortality was 7.5. Workers on the tops of the coke ovens accounted for the greatest part of this excess, observed and expected deaths from lung cancer in this group being 19 and 2.6, resp. Ninety percent of the coke oven workers studied were nonwhite; the excess risk for oven workers, and especially for topside oven workers, therefore explains the apparent excess lung cancer mortality among nonwhite steelworkers. Lung cancer mortality for whites and nonwhites employed at stations other than the top of the coke oven shows no nonwhite excess. Workers employed for 5 yr or more at topside coke oven jobs were found to be at a 10 times higher risk than others; in the long-term coke oven groups observed and expected deaths from lung cancer were 15 and 1.5, resp. An excessively high risk of digestive cancer was thought to have been observed among nonoven area workers.

1370 BENZENIC HYDROCARBONS AND SEVERE HEMOPATHIES. (Fr.) Girard, R. (Fac. Med. Lyon, France), F. Tolot and J. Bourret. *Arch Mal Profession* 31(12):625-636, 1970.

History of exposure to benzene or toluene was sought in 401 cases of serious blood dyscrasia and in 124 patients without hemopathic conditions drawn from the same population. In cases where there was a suspicion of significant exposure to benzene or toluene, the product of the factory in which the subject worked and the air in the factory were analyzed. Twenty percent of patients with medullary aplasia were found to have undergone exposure to benzene or toluene; 13.6% of patients with acute leukosis and 14.7% of patients with chronic lymphoid leukemias had toxic exposure to benzene or toluene. Four percent of patients without hemopathic conditions had histories of significant exposure to benzene or toluene. The danger of toxic exposure to benzene or toluene was thought to be greater in smaller industrial plants than in large ones, for the larger industries are more aware of the dangers of such exposure than are small enterprises such as dry cleaners, garages and builders.

- 1371 BILATERAL NON-FUNCTIONING THECOMA OF THE OVARY IN EPILEPTIC CHILDREN UNDER ANTICONVULSANT THERAPY. (E.) Schweisguth, O. (Inst. Gustave Roussy, Villejuif, France), R. Gerard-Marchant, B. Plainfosse, J. Lemerle, J. M. Watchi and P. Seringe. *Acta Paediat Scand* 60(1):6-10, 1971.

Two cases of bilateral ovarian thecoma in young children undergoing anticonvulsant therapy were observed. The patients were girls aged 5.5 and 3.5 yr. Both exhibited petit mal seizures for which they were given chemotherapy. In both cases the therapy included phenobarbital and phenacetylurea, and 1 girl was also given trimethadione, and the other was given diphenylhydantoin. Symptoms of tumor development, including bloody ascites, appeared 6 months after the start of anticonvulsant therapy in 1 case, and 4 months after the start of therapy in the other case. Neither patient showed signs of precocious sexual development. Both tumors showed gross areas of hemorrhagic infarction. A third case of bilateral ovarian thecoma associated with anticonvulsant therapy was found in the literature.

- 1372 EFFECT OF CYCLOHEXIMIDE ON THE LIVER CARCINOGENESIS PROCESS INDUCED BY DIETHYLNITROSAMINE. (Sp.) Alonso, A. (Ctr. Biol. Invest., U. Navarra, Pamplona, Spain). *Rev Esp Fisiol* 26(4):347-364, 1970.

- 1373 CILIARY ULTRASTRUCTURE IN THE DIETHYLSTIBESTROL INTOXICATED GOLDEN HAMSTER KIDNEY: ITS RELATION TO THE SO-CALLED HORMONE DEPENDENT DIFFERENTIATED NEPHROBLASTOMAS. (Sp.) Llombart, A., Jr. (Fac. Med. Valencia, Spain) and A. Peydro. *Med Esp* 64(379):235-241, 1970.

- 1374 LEUKOCYTIC ALKALINE PHOSPHATASE AND BENZENE EXPOSURE. (It.) Girard, R. (Inst. M. Lavoro, U. Lione, Italy), M. L. Mallein, J. Berthol, P. Couer and F. Tolot. *Med Lavoro* 61(10):502-508, 1970.

- 1375 REGRESSIVE MEDULLAR APLASIA AND FINAL ACUTE LEUKAEMIA AFTER CHLORAMPHENICOL TREATMENT (Fr.) Gadrat, J. (Toulouse Hosp., France), J. Monn, R. Bourse and J. Pris. *J. Med Chir Prat* 141(34-36):1155-1162, 1970.

- 1376 THE EFFECT OF AFLATOXIN B₁ ON THE MORPHOLOGY AND ENZYME ACTIVITY OF *MUCOR HIEMALIS* (MUCORALES). (Ger.) Reiss, J. (Grahamhaus Städt K., G., Bad Kreuznach, Germany). *Mycopathologia* 42(3-4):225-231, 1970.

- 1377 INDUCTION OF LYMPHOCYTE TRANSFORMATION BY PERIODATE. (E.) Novogrodsky, A. (Weizman Inst. Sci., Rehovot, Israel) and E. Katchlaski. *FE Letters* 12(5):297-300, 1971.

- 1378 MULTIPLE BREAST FIBROADENOMAS IN WOMEN ON HORMONAL CONTRACEPTIVES. (E.) Wiegenstein, L. (U. Washington Sch. Med., Seattle), R. Tank and V. E. Gould. *New Eng J Med* 284(12):676, 1971.

See also:

- * (Rev): 1275, 1277, 1285
- * (Phys): 1399, 1400
- * (Viral): 1424, 1451, 1463
- * (Immun): 1539, 1540, 1541, 1547, 1550, 1551, 1552
- * (Path): 1597
- * (Epid-Biom): 1611, 1623

PHYSICAL CARCINOGENESIS

- 1379 PATHOLOGIC EFFECTS OF DIFFERENT DOSES OF RADIOSTRONTIUM IN MICE: CHANGES IN THE HAEMATOPOIETIC SYSTEM. (E.) Nilsson, A. (Res. Inst. Natl. Defence, Sundbyberg, Sweden). *Acta Radiol* 9(6):528-544, 1970.

Quantitative, qualitative and time-dependent effects of various doses of radiostrontium on the hemato-poietic system in four groups of CBA male mice were studied. General depletion of all hematopoietic tissues occurred in all dose groups with a high frequency of aplasia in the 1.6 μ C group. The weight of the thymus diminished increasingly and the weight of the spleen increased progressively with increasing doses; an accentuated granulocytopoiesis occurred in which a discernible shift in relative proportions of granulocytes and lymphocytes in peripheral blood was noted. Involution of the thymus was accelerated and the spleen served to compensate for diminished bone marrow function with increasing doses. A difference in interrelationship of thymus, bone marrow and spleen may be involved in the differences in leukemogenesis between strontium irradiation and fractionated external irradiation.

- 1380 THE RESPONSE OF HAEMOPOIETIC COLONY FORMING UNITS TO SINGLE AND SPLIT DOSES OF γ -RAYS OR D-T NEUTRONS. (E.) Hendry, J. H. (Christie Hosp., Manchester, England) and A. Howard. *Int J Radiat Biol* 19(1):51-64, 1971.

The response of colony-forming units (CFU) of hemopoietic stem cells in the mouse femur to a single dose of D-T neutron irradiation of ^{137}Cs γ -ray irradiation was investigated by irradiating mice with a range of γ -ray or neutron doses, removing their femora, and assaying CFU. Split-dose response was examined by giving mice 2 doses of 200 rads of γ -rays separated by 2-24 hr; the survival of femoral CFU was compared with survival of a single dose of 400 rads. Survival curves for γ -rays were $D_0=85.7 \pm 4.5$ rads, extrapolation number = 3.1 ± 0.7 , and for neutrons, $D_0=58.1 \pm 3.4$ rads, extrapolation number = 1.7 ± 0.5 . Dose-fractionation of γ -rays in split dose experiments appeared to have a sparing effect on CFU, and survival curves obtained at various times after a first dose of 200 rads of γ -rays showed that a significant shoulder had reappeared within 5 hr of the first dose. When survivors were irradiated at 5, 8, or 20 hr after an initial 200 rad dose of γ -rays, a trend toward higher D_0 values was seen indicating increased radioresistance. Split dose fractionation of neutron irradiation had no sparing effect on femoral CFU.

- 1381 ^{90}Sr -INDUCED OSTEOSARCOMAS IN RADIATION CHIMAERAS. (E.) Barnes, D. W. H. (Med. Res. Counc., Radiobiol Unit, Harwell, Berkshire, England), T. E. F. Carr, E. P. Evans and J. F. Loutit. *Int J Radiat Biol* 18(6):531-537, 1970.
- The potential role of bone-marrow in the induction of osteosarcomata was tested by injection of syngeneic CBA/CBA-T6T6 and allogeneic CBA-T6T6/A chimeras with strontium-90 (20 μ C i.p.). Of the syngeneic chimeras, 2 of 13 animals died within 6 months before

tumors might be expected; 2 died at 10 months and were too autolysed for analysis; two died at 11 and 16 months, resp. of bone tumor and 7 with evident tumors were sacrificed. On cytological examination, 4 of 7 primary tumors contained aneuploid cells originating from the host; 2 of the primary tumors yielded only euploid cells of donor origin with T6T6 which, with passage, resulted in tumor lines with aneuploid chromosomes but without T6T6; one gave no cytological results, but on passage was shown to be aneuploid of host type without T6T6. Of the allogeneic chimeras, 4 of the 10 died after 9-11 months without evident tumors; 1 died after 9 months with osteoblastic tumor of the jaw; 5 were sacrificed for cytological study of tumors and were ultimately diagnosed in the first or subsequent passages as being of host origin and were aneuploid with 2 or more T6 chromosomes. In no case were the tumors established in A strain mice, though all grew progressively in CBA and (CBA-T6T6xA) F_1 . Eleven of 14 tumors induced with strontium-90 in normal mice all showed aneuploidy upon cytological examination. Most of the bone-tumors in both chimeras and normal animals were apparently endosteal in origin, resulting in bone-formation.

- 1382 OSSIFYING FIBROMA OF THE JAWS IN MICE AFTER INCORPORATION OF Ra-224 (THORIUM X). (Ger.) Luz, A. (Inst. Radiat. Res., Neuherberg, Germany) and B. Hindringer. *Verhandl Deutsch Ges Path* 54: 450-454, 1970.

The effects of long-term incorporation of Ra-224 in 2100 NMRT mice were found to induce osteoblastic sarcomas in various sections of the skeleton in 10% of the animals observed. However, a much greater proportion revealed ossifying fibroma of the jaws, mainly in the periosteal region. These changes were found in response to doses of 25 μ C/kg, were dose dependent and reached an 80% incidence at a dose of 50 μ C/kg of Ra-224. Enzyme histochemical studies showed the osteoblastic sarcomas and the ossifying fibromas to be distinguishable from each other. Alkaline phosphatase activity in ossifying fibromas was limited to the periosteum, whereas osteoblastic sarcomas were characterized by equal alkaline phosphatase activity in all the tumor cells. Two distinct types of tumors seemed to be caused by Ra-224.

- 1383 STUDIES ON THE IRRADIATION EFFECTS ON NORMAL ORGANS: IV. THE INFLUENCES OF γ -RAY IRRADIATION ON CAPILLARIES OF SMALL INTESTINE IN MICE. (Jap.) Fujiwara, K. (Sch. Med. Tokushima U., Japan). *Nippon Acta Radiol* 30(6):550-554, 1970.

A single dose of whole body γ -ray irradiation (1000 r at 50 r/min) produced partial narrowing, dilatation and increased permeability of capillaries in the small intestine in mice by 3 hr postirradiation. By 1-3 days postirradiation, these changes had become more conspicuous. When a 1800 r dose of γ -ray irradiation was fractionated into 6 or 18 separate doses over a period of 3 wk, it appeared that changes in intestinal capillaries were less pronounced than in animals given the lower single dose.

- 1384 THE RESPONSE OF THE SKIN OF SWINE TO INCREASING ABSORBED DOSES OF THE $^{10}\text{B}(\text{n},\alpha)^7\text{Li}$ REACTION: HISTOLOGIC AND CYTOLOGIC CHANGES. (E.) Archambeau, J. O. (Nassau Cty. Med. Ctr., East Meadow, N. Y.). *Radiat Res* 45(1):137-144, 1971.

Changes in the skin of swine given 950 or 1250 rads of irradiation from the $^{10}\text{B}(\text{n},\alpha)^7\text{Li}$ reaction were investigated. Two female swine were given an i.v. injection of 35 mg of boron/kg body wt followed by irradiation of a 10 cm area of the shoulder with thermal neutrons. Erythema and epilation were observed after 950 or 1250 rads. After 950 rads, there was a progressive loss of cells and thinning of the epidermis with leakage of serum and crust formation; the epidermis regenerated in 20-27 days, and the lesion healed. Following 1250 rads a similar reaction occurred, but the lesion did not heal. The nuclear volumes of basal and prickle cells increased 100% by 14 days after irradiation with 1250 rads; with 950 rads, the nuclear volumes of basal and prickle cells increased to 400% in 21 days. The mitotic index of cells at 5, 10 and 15 days after 1250 rads was zero. With 950 rads, the percent of abnormal mitoses had increased to 6% by day 7, and then the percent of abnormal mitoses dropped to 0% on day 20 and rose to 1.8% on day 27 after irradiation. An increase in capillary diameter followed irradiation in both amounts. Whereas nuclear volume and mitotic index were at control levels in swine exposed to 950 rads by 27 days postirradiation, capillary diameters continued to increase in this group.

- 1385 THE RESPONSE OF THE SKIN OF SWINE TO INCREASING ABSORBED DOSES OF RADIATION FROM A THERMAL NEUTRON BEAM. A DEGRADED FISSION NEUTRON BEAM, AND THE $^{10}\text{B}(\text{n},\alpha)^7\text{Li}$ REACTION. (E.) Archambeau, J. O. (Nassau Cty. Med. Ctr., East Meadow, N. Y.), R. G. Fairchild and H. J. Brenneis. *Radiat Res* 45(1):145-165, 1971.

A moist reaction produced in the skin of immature female and castrated male Hampshire swine is quantified following increasing absorbed doses from a thermal neutron and a degraded fission beam. After single exposures, erythema occurred during the first week inconstantly and variably with epilation appearing early during the second week, progressing to a moist reaction first seen in the third week and reaching completion between the fourth and sixth weeks. Time of epilation was 9.0 days and was complete by 31.2 days with changes being dose independent, and regrowth of hair occurred at absorbed doses of the order of 1000 rads. A moist reaction occurred in response to the thermal neutron beam in all fields over the dose range from 906-2247 rads ranging from small to progressively larger areas, and healing occurred prior to 49 days with 1446 rads or less. With the fission neutron beam a moist reaction occurred in all fields over the dose range from 350-1450 rads, progressing to larger areas with dose increase; healing occurred prior to 49 days at doses below 800 rads. A moist reaction occurred in 20 of 21 fields over the dose range of 865-2000 rads with the $^{10}\text{B}(\text{n},\alpha)^7\text{Li}$ reaction, with varying degrees of healing noted by day 49. The reduced biologic effect of the thermal neutron

beam is explained by the presence of a large gamma concentration.

- 1386 STIMULATED UPTAKE OF α -AMINOISOBUTYRIC ACID IN RAT LIVER FOLLOWING WHOLE BODY γ -IRRADIATION. (E.) Shihabi, Z. (Gen. Hosp. Buffalo, N. Y.) and O. W. Neuhaus. *Radiat Res* 45(1):202-209, 1971.

The effect of irradiation on amino acid incorporation by the liver was studied by following the uptake of ^{14}C - α -aminoisobutyric acid (AIB) in livers taken from rats exposed to 1300 R of γ -irradiation. When liver homogenates of irradiated rats were incubated with ^{14}C -labeled AIB, 17% of the labeled AIB was taken up by 48 hr after irradiation and 37% by 96 hr. In pair-fed unirradiated controls on the other hand, labeled AIB incorporation at 48 and 96 hr post-infection was 7 and 8%, resp. The striking increase in uptake of AIB after irradiation was apparently confined to the liver, and at the expense of other organs. Kidney, muscle, spleen and testes showed decreased amounts of label following irradiation. Treatment with aminoethylisothiuronium and cysteamine to some extent decreased AIB uptake following irradiation. Irradiation also increased hepatic uptake of radioactive phosphorus and algal hydrolysate, but inulin uptake and orotic acid uptake were not affected.

- 1387 ESTERASE ACTIVITY AND PROTEIN CONTENT OF PLASMA AND ERYTHROCYTES OF TOTALLY IRRADIATED RATS. (Ger.) Valet, G. (Max Planck Inst Biochem., Munich, Germany) and G. Ruhenstroth-Baue. *Strahlentherapie* 140(6):738-744, 1970.

Groups of 10 rats received total body irradiation 500 R, were exsanguinated (at different times), and the blood prepared for analysis. Blood volume, hematocrit, plasma protein concentration and plasma esterase activity were determined. The results revealed that there was a loss of protein following radiation, which was related to a decrease in total proteins and plasma volume; the plasma protein concentration was at first unchanged and dropped only after the 4th day following irradiation. The initial values were first regained by the plasma volume, followed by the total protein, and lastly the protein concentration, which was maintained for the longest time interval. The plasma esterase specific activity increased over the initial value between the 1st and 3rd day following irradiation, although the esterase activity/total plasma declined; there was a decrease in esterase activity over the 18 day interval following radiation for all pH values. Volume protein content and protein concentration of the erythrocytes were not significantly changed within the experimental interval.

- 1388 DNA REPAIR AND RADIATION SENSITIVITY IN HUMAN (XERODERMA PIGMENTOSUM) CELLS. (E.) Cleaver, J. E. (Lab. Radiobiol., U. California, San Francisco). *Int J Radiat Biol* 18(6):557-565, 1970.

This study was designed to assess *in vitro* sensitivity of the colony-forming ability of xeroderma pigmentosum fibroblasts as compared to that of normal fibroblasts and the levels at which repair replication is detectable utilizing punch biopsies from the forearms of patients and volunteers. Repair replication was detected in both normal, heterozygote and homozygote fibroblasts with quantitative measurements obtained at the level of 220 ergs/mm²; there appeared to be 0-25% of the normal repair in xeroderma pigmentosum cells with no simple difference between the levels of repair in the two forms. The ability of xeroderma pigmentosum cells to form colonies after ultraviolet irradiation was reduced and survival curves for both cell-types appeared to be exponential; regression lines calculated with all data points gave $n=1.0$, $d_0=29$ ergs/mm² (correlation coefficient of 0.989) for normal cells, $n=0.9$, $D_0=9$ ergs/mm² (correlation coefficient of 0.995) for abnormal cells. Xeroderma pigmentosum, in which malignancy is correlated with low repair, may illustrate a special restricted mechanism of carcinogenesis.

- 1389 RADIOSENSITIVITY OF MAMMALIAN CELLS: IV. CHANGE OF DNA CONTENT IN NUCLEI OF RAT SOMATIC CELLS AFTER IRRADIATION. (E.) Kobayashi, J. (Sch. Med. Tokushima U., Japan). *Tokushima J Exp Med* 17:47-55, 1970.

The effect of irradiation on DNA content of rat embryo somatic cells (Wistar strain) after a dose of 500 R was studied, utilizing spectrophotometry to determine DNA content of individual nuclei. Liver nuclear DNA content was most markedly decreased after 10 hr irradiation, with normal distribution regained 20-25 hr after exposure. In kidney cells, the average DNA content per nucleus decreased 5-10 hr after irradiation to a low of 88-90% of control values and returning to normal within 15-20 hr. In brain cells, the average DNA content decreased after 5-15 hr and returned to normal after 20-25 hr. Distribution frequencies of cells with below control DNA content showed peak values at 10 hr for liver cells and 5 hr for kidney and brain cells. Present data suggest that the decrease of the DNA content in somatic cells was associated with physicochemical changes of Feulgen-positive DNA in nucleoproteins.

- 1390 RADIOSENSITIVITY OF MAMMALIAN CELLS: V. DNA SYNTHESIS IN MOUSE SOMATIC CELLS AND TUMOR CELLS *IN VITRO* AFTER IRRADIATION. (E.) Kobayashi, J. (Sch. Med. Tokushima U., Japan). *Tokushima J Exp Med* 17:105-107, 1970.

DNA synthesis in mouse kidney, liver and Ehrlich tumor cells of Swiss albino mice was studied *in vitro* by measuring ³H-thymidine incorporation after an X-irradiation dose of 500 R. Incubation for 30 min showed an increase in label incorporation with a subsequent decrease of 50% within 1 hr followed by an increase to control levels within 24 hr with kidney cells. In liver cells, a similar pattern was noted, but a more gradual decrease after 1 hr of irradiation occurred; in Ehrlich cells, label was

found in 49.1% of cells after 30 min, 24.6% after 1 hr and 12.8% after 5 hr. These results show that inhibition of DNA synthesis by irradiation is similar in somatic and tumor cells.

- 1391 RELATION OF X-RAY-INDUCED THYMIDINE UPTAKE TO CHROMOSOME REVERSION AT PROPHASE IN GRASSHOPPER NEUROBLASTS. (E.) Thornton, J. (U. Texas Southwestern Med. Sch., Dallas) and M. E. Gauden. *Int J Radiat Biol* 19(1):65-78, 1971.

Unscheduled DNA synthesis in the grasshopper neuroblast of embryo cultures at prophase have been studied through identification of X-ray induced thymidine uptake, using autoradiograms for re-identification. The initial-late prophase was the latest point in the cell cycle of the neuroblast at which unscheduled DNA synthesis occurred with X-irradiation of 500-1000 R. Thymidine uptake induced by 32 R of X-rays in the latter part of prophase occurred only in reverted cells under isotonic conditions indicating reversion of recondensation in the chromosome. Slightly hypotonic medium increased thymidine uptake induced by 32 R of reverted and delayed cells. Some degree of chromosome decondensation appears to be a necessary but not sufficient condition for induction of radiation-induced ³H-thymidine uptake by neuroblasts.

- 1392 THE RATE OF TRANSLOCATIONS INDUCED IN SPERMATOGONIA OF MICE BY TWO X-IRRADIATION EXPOSURES SEPARATED BY VARYING TIME INTERVALS. (E.) Leonard, A. (C.E.N.-S.C.K., Mol, Belgium) and G. Deknutt. *Radiat Res* 45(1):72-79, 1971.

The induction of translocations in the spermatogonia of mice by 2 successive exposures to X-irradiation was investigated. Male mice were given 250 r of X-irradiation followed 1-10, 16 or 24 hr later by another 250 r dose; other rats were given a single 500 r dose, or a single 250 r dose. Between 80-100% of spermatocytes undergoing translocations showed 1 translocation; 1-10% had 2 or 3 translocations. Eight percent of spermatocytes showed translocations following a single 500 r dose, and 4.25% showed translocations following a single 250 r dose. Maximum percentages of cells showing translocations were attained when the second X-ray dose followed the first by 16 hr (8.40% of spermatocytes showing translocations). The minimal proportion of cells showing translocations (4.44%) was reached when the time interval between doses was 7 hr. Percentages of cells showing translocations continued to rise and fall with the interval between X-ray doses, without showing a prolonged increase or decrease. The results may represent a differential susceptibility to radiation of cells in various cycle-stages.

- 1393 MAMMALIAN CELL GENETICS: III. CHARACTERIZATION OF X-RAY INDUCED FORWARD MUTATIONS IN CHINESE HAMSTER CELL CULTURES. (E.) Chu, E. H. Y. (Oak Ridge Natl. Lab., Tenn.). *Mutat Res* 11(1):23-34, 1971.

The mutagenic effects of X-irradiation of the gene controlling 8-azaguanine (8-AG) sensitivity was investi-

gated in cultures of Chinese hamster cells. X-Irradiation induced forward mutations from 8-AG sensitivity to resistance. Cells were given varying doses of X-irradiation followed 42 hr later by treatment with 8-AG; cell survival decreased directly with increasing dose of X-irradiation. Cell density affected frequency of forward mutations in irradiated cells; the optimal inoculum for mutation was 1.25×10^5 cells/100 mm culture plate. Lower densities did not increase the final yield of 8-AG resistant mutations. Frequency of mutations/ 10^5 surviving cells increased from 1.5 for cultures not given X-irradiation to 11.4 for cultures given 400 r, and 16.0 for cultures given 800 r; above 800 r, the frequency of mutations declined to $7.5/10^5$ cells at 1200 r. In another experiment, a non-linear increase in the frequency of forward mutations was observed to accompany increasing dose of X-irradiation, the rate of induced mutations ranging from 4.2×10^{-7} to 1.8×10^{-6} mutations for 200 r and 1200 r, resp. Seventy-two 8-AG resistant mutants were tested for their ability to revert to 8-AG sensitivity; the test cells were treated with N-methyl-N'-nitro-N-nitrosoguanidine and other agents. Mutants reverted to 8-AG sensitivity after treatment with different chemical mutagens, suggesting that both point mutations and chromosome deletions may have occurred in hamster cells after exposure to ionizing radiation.

- 1394 METAPHASE CHROMOSOME ABBERATIONS IN CHINESE HAMSTER LIVER CELLS *IN VIVO* AFTER SINGLE ACUTE ^{60}Co EXPOSURE. (E.) Brooks, A. L. (Lovelace Found. Med. Educ. Res., Albuquerque, New Mexico), R. F. Peters and M. D. Rollag. *Radiat Res* 45(1):191-201, 1971.

The induction of metaphase chromosomal aberrations by ^{60}Co irradiation was investigated *in vivo* in Chinese hamster liver cells. Hamsters were exposed to 150 R whole body ^{60}Co irradiation 1 hr before, or 24 and 48 hr after, partial hepatectomy; in other experiments, animals were given differing doses of radiation. The total number of chromosome breaks/cell scored at the 3 exposures was similar, ranging from 0.09-0.13 breaks/cell; this appeared to suggest that liver cell chromosomes have about the same sensitivity to the induction of abberations at all stages of the cell cycle. The type of abnormalities observed did change relative to the time of exposure to ^{60}Co irradiation. At 1 hr before and 24 hr after hepatectomy, chromosome-type abnormalities were found, while at 48 hr after hepatectomy, chromatid-type abnormalities predominated. By 22 hr after hepatectomy, DNA synthesis, measured by uptake of ^{14}C -thymidine in liver cells was observed; ^{14}C -thymidine incorporation peaked at 28 hr after hepatectomy and remained near maximal levels through 52 hr after hepatectomy. Animals partially hepatectomized 1 hr or 7 days after exposure to irradiation showed no significant differences in the total number of aberrations/cell. Dose-response curves for metaphase abberations indicated that liver cells were more resistant to radiation-induced abberations than testis or bone marrow tissue. The frequency of abberations increased as a function of time after partial hepatectomy; by 40 hr after hepatectomy,

hamster liver cells exposed to 250 R showed .09 abberations/cell and by 54 hr after hepatectomy, the number of abberations/cell was .17. The increase represented an increase in deletions; the frequency of rings and dicentrics remained unchanged.

- 1395 RECTAL REACTION FOLLOWING RADIATION THERAPY OF CERVICAL CARCINOMA: PARTICULAR REFERENCE TO SUBSEQUENT OCCURRENCE OF RECTAL CARCINOMA. (E.) MacMahon, C. E. (U. Washington Med. Sch., Seattle) and J. M. Rowe. *Ann Surg* 173(2):264-269, 1971.

Six cases of carcinoma developing in the rectum and recto-sigmoid following radiation treatment of cervical cancer were reported. The patients ranged in age from 25-65 yr, and the time elapsed from irradiation to onset of rectal tumors was 14 months to 25 yr. Tumors were adenocarcinomas of the rectum and/or recto-sigmoid in 5 cases, and papillary adenocarcinoma of the rectum in 1 case. Tumors invaded the muscle in 2 cases and the muscle and serosa in 3 cases.

- 1396 NEOPLASMS AFTER CHILDHOOD IRRADIATION OF THYMUS GLAND. (E.) Janower, M. L. (Massachusetts Gen. Hosp., Boston) and O. S. Miettinen. *JAMA* 215(5):753-755, 1971.

The association of childhood diagnostic irradiation of the thymus and subsequent development of neoplasms was investigated in 511 irradiated children, 532 unirradiated children, the siblings of the irradiated children and the siblings of the unirradiated controls. The age at admission to the study was 4.7 yr for the irradiated children; and the mean age at the termination of the study was 34.8 yr. Fifty-seven percent were male and most were from low socioeconomic backgrounds. Patients were given total doses of 400 roentgens of irradiation. In the irradiated patients, there were 2 malignant and 9 benign thyroid neoplasms; no malignant thyroid neoplasms were observed in any of the irradiated groups, and the numbers of benign thyroid tumors in these groups totalled 10. The malignant thyroid tumors in the irradiated children were follicular carcinomas and a papillary cystadenocarcinoma; the tumors were principally adenomas. In the irradiated group, malignant neoplasms of organs other than the thyroid included 1 case of malignant lip tumor, 1 case of malignant brain tumor, 1 case of malignant cervical tumor, 1 case of disseminated lymphosarcoma, 1 case of acute myelocytic leukemia, and 3 cases of mammary carcinoma. Siblings of irradiated and unirradiated children showed no appreciable differences in tumor development.

- 1397 REPORT ON PATHO-ANATOMICAL AND RADIOAUTOGRAPHIC STUDIES OF NINE CASES OF HUMAN THOROTRASTOSIS. (Ger.) Wegener, K. (Path. Inst. U. Heidelberg, Germany) and R. Zahnert. *Virchow Arch Path Anat* 351(4):316-332, 1970.

Investigations dealing with thorotrast injections are described, including morphological and autoradiographic studies.

graphic studies and the quantitative determination of the thorotrast and its metabolic products. The thorotrastosis cases were divided into 3 different groups: Group I - organs and tissues with thorotrast storage and with delayed injury including the liver, spleen, lymph nodes, bone marrow and paravascular tissues in the area of the injection site; Group II - organs and tissues with thorotrast storage but without delayed injury including the kidneys, adrenals, tonsils, gastrointestinal tract, hepatic duct, fatty tissue, gallbladder, urinary bladder, lungs, pancreas, pleura, prostate, thyroid, vertebral discs, and testes; and Group III - organs and tissues without thorotrast uptake or late injuries including arteries and veins, bronchi and trachea, central nervous system sections and spinal column, the heart, skin, various musculature, peritoneum, and nails. The administration of thorotrast was undoubtedly responsible for liver cirrhosis in 9 cases and liver malignancies in 7 cases.

1398 LEUKEMIA IN ATOMIC BOMB SURVIVORS, HIROSHIMA AND NAGASAKI, 1 OCTOBER 1950-30 SEPTEMBER 1966. (E.) Ishimaru, T. (Nat'l. Inst. Hlth., Hiroshima, Japan), T. Hoshino, M. Ichimaru, H. Okada, T. Tomiyasu, T. Tsuchimoto and T. Yamamoto. *Radiat Res* 45(1):216-233, 1971.

The incidence of leukemia developing among survivors of the atomic bomb attacks on Hiroshima and Nagasaki, Japan, was investigated in fixed cohorts of survivors. The risk of developing leukemia was substantially greater among those exposed to significant doses of radiation. In Hiroshima, annual leukemia incidence rates/100,000 population for those exposed to 200, 300, and 400 rads of bomb radiation were 58, 80, and 120 cases, resp. In Nagasaki, the incidence of leukemia in those exposed to 200, 300, and 400 rads was 38, 68 and 78, resp. The differences in incidence in the 2 cities may reflect differences in the kind of radiation emitted by the bombs, or errors in dosimetry, or other differences between the 2 cities. The relative risk of developing leukemia in both Hiroshima and Nagasaki was greater for males than for females, especially in the high dose region. The risk of leukemia was found to be lower in persons over 40 yr of age at the time of the bombings than in younger persons. The risk of leukemia among bomb survivors declined with time after the bombings, especially among those exposed to 100 rads or less. It was found that in Hiroshima persons exposed to 5-99 rads had increased risks for acute lymphocytic leukemia and chronic granulocytic leukemia, but not for acute granulocytic leukemia.

1399 OCCUPATIONAL FACTORS IN THE EPIDEMIOLOGY OF LEUKEMIA IN HIROSHIMA AND NAGASAKI. (E.) Ishimaru, T. (Japanese Nat'l. Inst. Hlth., Hiroshima), H. Okada, T. Tomiyasu, T. Tsuchimoto, T. Hoshino and M. Ichimaru. *Amer J Epidemiol* 93(3):157-165, 1971.

The incidence of leukemia among citizens of Hiroshima and Nagasaki, Japan in various occupational groups was investigated; subjects included persons exposed to

atomic bomb irradiation in 1945 and persons not so exposed. Occupational exposure to X-irradiation and/or benzene as a solvent were found to be associated with a risk of developing leukemia on the order of 2.5 times higher than the risk of unexposed subjects. Especially high risks were found for welders, sheet metal workers, cabinet makers, rubber products workers, glass workers, barbers and radiologists. The effect of atomic bomb irradiation exposure and history of occupational exposure to benzene or medical X-rays was also investigated. The heavily bomb radiation-exposed group (exposed to 100 rads or more) which had occupational exposure to benzene or X-rays had a relative risk of developing leukemia of 1.5; the low bomb-irradiation dose group had a risk of 4.0; the unirradiated group had a risk of 2.4. In all groups exposed to atomic-bomb irradiation, risks of developing leukemia were higher in persons with histories of occupational exposure to benzene or X-irradiation.

1400 THE THORIUM-SERIES IN CIGARETTES AND IN LUNGS OF SMOKERS. (E.) Joyet, G. (Lab. Dosimetry Protection, U. Zurich, Switzerland). *Experientia* 27(1):85-89, 1971.

The accumulation of radioactive thorium (^{232}Th) in the lungs of cigarette smokers was investigated. The thorium-equivalent wt for smoke produced by 9000 cigarettes (the annual consumption of a heavy smoker) was calculated for 8 brands of British, American, and French cigarettes, and found to range from 9-36 mg. The thorium-equivalent wt in the lungs of 10 cigarette smokers and 2 nonsmokers were also calculated. Four smokers had no measurable thorium in their lungs, and 6 had thorium wt of 0.8-2.4 mg. The 2 nonsmokers had no detectable thorium in their lungs. Although the toxic effects of thorium in the lungs of smokers was not investigated, it was reported that 2 workers having occupational exposure to thorium vapor developed incapacitating dyspnea with fibrosis.

1401 APPEARANCE OF SKIN HEMANGIOMA 15 YEARS AFTER RADIATION LESION. (It.) Donati, E. (City Hosp. U. Verona, Italy). *Minerva Radiol* 15(7-8):207-212, 1970.

1402 ELECTRON MICROSCOPIAL STUDY OF TWO TRAUMATIC NEUROMAS. (Fr.) Ferriere, G. (Hosp. Salpetriere, Paris, France), J. Poirier and R. Escourolle. *Ann Anat Path* 15(3):347-360, 1970.

1403 KINETICS OF DISTRIBUTION AND EXCRETION OF RADIUM ISOTOPES AFTER INTRAVENOUS INJECTION OF THOROTRAST. (Ger.) Kaul, A. (Steglitz Clin., Free U. Berlin, Germany) and J. Heyder. *Biophysik* 71(1):74-84, 1970.

1404 KIDNEY THOROTRASTOSIS AFTER ASCENDENT
PYELOGRAPHY. (It.) Falzi, G. (U. Milan
Inst. Legal Med., Italy), A. Ritucci and A. Russo.
Gass Sanit 41(7-8):325-334, 1970.

1405 DOSIMETRY OF ^{90}Sr AND ^{90}Y IN THE RAT FEMORAL
MEDULLARY CANAL AFTER INTRAVENOUS ADMINIS-
TRATION. (Ger.) Steinbach, K. H. (Heiligenberg Inst.,
Germany) and E. Weber. *Strahlentherapie* 140(6):667-
670, 1970.

1406 FORMATION OF LUNG CARCINOMA DUE TO INTRA-
PULMONARY FOREIGN BODIES. (Ger.) Pomplun,
S. (Zschadrass Clin Tuberculosis and Lung Dis.,
Germany). *Z Erkrank Atmungsorg* 132(3):257-262, 1970.

1407 HISTOLOGICAL AND HISTOCHEMICAL OBSERVATIONS
ON THE ADRENALS OF RATS AFTER LOCAL AND
WHOLE BODY IRRADIATION. (Ger.) Unger, E. (Frederic
Joliot Curie St. Res. Inst. Radiobiol. Radiohyg.,
Budapest, Hungary). *Radiobiol Radiother* 116(6):737-
748, 1970.

1408 OSTEOGENIC SARCOMA ARISING IN A PREEXIST-
ING FIBROUS DYSPLASIA: REPORT OF A CASE.
(E.) Slow, I. N. (Mt. Sinai Sch. Med., City U. New
York, N. Y.), D. Stern and E. W. Friedman. *J Oral
Surg* 29(2):126-129, 1971.

1409 RESPONSE OF MOUSE EPIDERMAL CELLS TO SINGI
AND DIVIDED DOSES OF FAST NEUTRONS. (E.)
Denekamp, J. (Roy. Postgrad. Med. Sch., London,
England), E. W. Emery and S. B. Field. *Radiat Res*
45(1):80-84, 1971.

1410 BONE TUMORS INDUCED BY STRONTIUM 90. (Fr.)
Graf, B. (Ctr. Nucl. Stud., Fontenay-aux-
Roses, France), J. Lafuma, C. Parmentier and N.
Parmentier. *Bull Cancer* 57(3):381-396, 1970.

See also:

- * (Rev): 1277
- * (Chem): 1295
- * (Viral): 1424
- * (Immun): 1544, 1573
- * (Epid-Biom): 1610

VIRAL CARCINOGENESIS

- 1411 PULMONARY ADENOMATOSIS OF SHEEP (JAAGSIEKTE): I. ULTRASTRUCTURE OF THE TUMOR. (E.) Perk, K. (Hebrew U., Rehovot, Israel), I. Hod and T. A. Nobel. *J Nat Cancer Inst* 46(3):525-537, 1971.

Pulmonary adenomas from Asassi sheep with pulmonary adenomatosis (jaagsiekte) were examined by electron microscopy and found to be composed of cells apparently derived from type B alveolar epithelial cells. Cells of advanced tumors had abundant collagen; some cells were so impregnated by collagen fibers as to cause lysis. Many of the tumor cells, as well as normal ovine B type alveolar cells, were characterized by dense osmiophilic "cytosomes" consisting of concentric or parallel lamellae. Cytosomes were more numerous and larger in adenomas than in normal cells. Glycogen granules, absent in normal alveolar cells, were common in tumor cells. free ribosomes in the form of polysomal aggregates were found in tumor cells, but not in normal cells. Golgi complexes were more extensively developed in tumor cells than in most normal cells, and only in tumor cells were there large cytoplasmic clefts and many filaments in the cytoplasmic matrix. Virus particles, though rare, were seen occasionally in the cisternae of the granular endoplasmic reticulum; cisternal viral buds were also seen.

- 1412 IN VITRO STUDIES OF RAT VIRUSES: I. EFFECTS OF LONG-TERM CULTURE. (E.) Lum, G. S. (VA Hosp., Cincinnati, Ohio). *Oncology* 24(6):401-415, 1970.

Rat embryo cells cultured for up to 5 yr (78 cell passages) showed no marked morphological differences from primary passage cells; the long-term passage cells produced only 1 tumor in 52 inoculations when inoculated into rats, that tumor being produced by cells from a 16 month-old culture. When the susceptibility to viral infection of long-term culture cells was tested, it was found that cells remained susceptible to infection by rat viruses (strains RV and L-S) through passage 33; however, resistance to infection increased in long-term cell cultures, and no cytopathic effect was seen in long-term cultures. Cells surviving persistent virus infection were maintained in long-term cultures. Some of these cultures produced virus for as long as 2 yr before becoming virus-negative, while others produced virus in cycles of varying durations; 1 culture produced virus from day 20-50, from day 70-90, from day 400-420, and from day 700-740. Some long-term cultures were resistant to re-inoculation, while others were susceptible to re-inoculation. Neutralization tests on virus released from inoculated cells after various periods of time under cultivation showed the virus to be identical to the virus used for the initial infection.

- 1413 VIRAL AND MORPHOLOGIC STUDIES ON HEPATOMAS IN MICE OF STRAIN C3H-A^{VV}, WITH OBSERVATIONS OF A CULTURED HEPATOMA. (E.) Maca, R. A. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), U. Heine and B. A. Manaker. *Arch Geschwulstforsch* 36(3):213-230, 1970.

Studies are reported on the etiology and morphological characteristics of spontaneously occurring hepatomas in C3H-A mice using complement-fixation histologic and electron microscopic techniques. The fine structure of tumor cells growing *in vivo* was found to be similar to that of normal hepatic cells of control animals. *In vitro* cultivation in one instance gave rise to clones of epithelioid cells surrounded by fibroblasts lacking many of the characteristic cellular features of hepatocytes. Subcutaneously transplanted tumor tissues showed regression in steroid-treated mice. A few virus particles of the "immature C-type" were found in extracellular spaces of primary or transplanted tumors, but virus particles were not seen in any hepatic tissue from 3 adult male mice free of hepatomas. Evidence of budding of particles at the cell membrane of hepatic cells was absent despite extensive examination. It is not known whether epithelioid cells or fibroblasts are the site of origin of the virus particles.

- 1414 VIRUS IN HUMAN CANCER AND LEUKEMIA. (E.) Awano, I. (Fukushima Med. Coll., Japan), M. Sanbe and H. Yoshida. *Tohoku J Exp Med* 102(3):233-263, 1970.

Biopsy materials from human cancer and leukemic tissue were examined by electron microscopy for the presence of virus particles. Virus-like particles were observed in the cytoplasm of metastatic lymph node carcinomas from patients with gastric and lung cancer. These were 100-150 mμ in size and had cores of 60-80 mμ. Mature C-type virus-like particles were found in the cytoplasm of leukemic cells of metastatic spleen and lymph node cancer cells from a patient with acute myelogenous leukemia. The cancer cells from stomach and lung cancer patients contained inclusions in the form of nuclear bodies and dense osmiophilic nuclear particles in the nucleus. Nuclear bodies were composed of small-granular cortical bands and pale homogeneous cores. The nuclear particles appeared to increase in size and develop into nuclear globules found in the nuclear body. The core of the virus-like particles in the cytoplasm may have derived from the nuclear particles. Doughnut-shaped particles were seen in the extracellular spaces between cancer cells in addition to the virus-like particles.

- 1415 TRANSFORMATION OF MOUSE EMBRYO CELLS BY VACCINA VIRUS. (E.) Kosiorowska, J. (Serum Vaccines Res. Lab., Warsaw, Poland), K. Wlodarski and N. Mazurowa. *J Nat Cancer Inst* 46(2):225-241, 1971.

Mouse embryo cells infected at low multiplicity (0.0001 plaque-forming U/cell) with vaccina virus developed low-grade infections in 90% of the cultures and 40% showed morphologic transformation. At the 12th passage level, about 90% of the transformed cells were chromosomally hypotetraploid, and 7% were hypodiploid and diploid. Morphologic examination and autoradiography revealed vaccina virus

present in the transformed cells. Tests for viral antigens with rabbit antiserum showed that vaccinia viral antigens were present in cells. Content of vaccinia antigens decreased in cells in later passages. Transformed mouse embryo cells were more resistant to superinfection than were untransformed cells. Tumorigenicity of cells in later passages was increased; tumors developed by mice injected with infected cells from early passage levels (2 wk) regressed, while tumors developed by mice injected with 62-65th passage level cells often proved fatal.

1416 FIBROSARCOMA AT THE SITE AND IMMEDIATELY FOLLOWING SMALL-POX VACCINATION. (E.)

Archampong, E. Q. (Ghana Med. Sch., Accra) and G. Clark. *Brit J Surg* 57(12):937-938, 1970.

A case of fibrosarcoma developing at the site of a smallpox vaccination was reported. The patient, a 44-yr-old woman from the Krobo State of Ghana, had received 3 smallpox vaccinations prior to the vaccination reported, which was administered by means of an injection gun apparatus. Three months after vaccination, a nodule developed at the vaccination site and was treated with cyclophosphamide. The tumor was excised twice, and it recurred both times. It was found to be a spindle-cell fibrosarcoma invading the subcutaneous tissue. While a direct association between the vaccinia and the development of the tumor was not demonstrable, the coincidence of the vaccination and the site and time of the tumor's development suggests a causal relationship between the two.

1417 THE DEVELOPMENT OF CHICK-EMBRYO-LETHAL-ORPHAN (CELO) VIRUS T AND V ANTIGENS IN LYTICALLY INFECTED CHICK KIDNEY CELLS. (E.) Anderson, J. (Baylor Coll Med., Houston, Texas), K. J. McCormick, W. A. Stenback and J. J. Trentin. *Int J Cancer* 7(1):59-64, 1971.

To determine the sequence of synthesis of tumor and virion antigens of chick-embryo-lethal-orphan (CELO) virus in lytically infected chick kidney cells, cultures were infected at 30 egg lethal doses (ELD₅₀). The antigens had been distinguished by their staining patterns; the tumor antigen was confined to the nucleus of infected cells and was morphologically similar to the SV40 tumor antigen; the virion antigen first appeared in the nucleus and then spread to cytoplasm. In lytically infected chick kidney cells, the indirect immunofluorescence test showed that tumor antigen developed 6 hr after infection and reached a peak of 90% antigen-positive nuclei at 20-24 hr postinfection. The virion antigen was detected 20 hr postinfection. The synthesis of both antigens was inhibited by cycloheximide, but only the virion antigen was inhibited by cytosine arabinoside. Tumor antigen in fixed cells could not be detected after storage for 3 wk in liquid nitrogen.

1418 A VIRUS OF HUMAN LEUKOSIS. (Rus.)

Barinskiy, I. F. (D. I. Ivanovskiy Inst. Virol., Moscow, U.S.S.R.), A. K. Shubladze, A. F. Bocharov, F. P. Filatov and I. v. Dement'yev. *Vop Virusol* 15(6):729-730, 1970.

Three strains of a human leukocytic leukemia virus (HLV) were isolated from leukocyte suspensions obtained from 5 leukemic patients. Inoculation of human leukocyte cultures with these HLV strains of the 5th passage increased the mitotic rates to 26, 20 and 16 per 1000, while the mitotic rates of a control culture or of a cell culture treated with a comparable fraction obtained from a healthy donor and passaged 4 times were 10 and 6 per 1000. The HLV strains exhibited poor stability; they were destroyed by ether and thermally inactivated at 60°C within 30 min. These strains were not pathogenic to laboratory animals such as rabbits, mice, rats, hamsters or guinea pigs. Differential centrifugation of HLV-infected cell culture homogenates in a CsCl gradient revealed that HLV had a buoyant density of 1.184 g/cm³ which corresponded to that of the avian or murine leukemia virus. Electron microscopy of these strains after gradient centrifugation revealed the presence of typical leukemia virus particles with a characteristic morphology. Viral particles were also noticed in the ultrathin slices of HLV-infected leukocytic cultures mainly in the cytoplasm. The structure and the parameters of these HLV strains were similar to those of the animal leukemia virus. The absence of β-globulins and a considerable increase in α₁-globulins were observed in the HLV-infected leukocytic cultures.

1419 SEARCH FOR A HUMAN BREAST CANCER VIRUS.

(E.) Moore, D. H. (Inst. Med. Res., Camden, N. J.), J. Charney, B. Kramarsky, E. Y. Lasfargues, N. H. Sarkar, M. J. Brennan, J. H. Bur S. M. Sirsat, J. C. Paymaster and A. B. Vaidya. *Nature* 229(5287):611-614, 1971.

Mammary milk from women from 3 distinct populations examined in order to locate viral particles similar to those found in the milk of mice with mammary tumors (B-type particles). The 3 populations were 156 women from the Philadelphia area with no family history of breast cancer, 10 women with histories of breast cancer in their families, and 46 women from the inbred Parsi community in Bombay, which has a high incidence of mammary cancer. Particles with the same morphological characteristics as those which are thought to cause breast cancer in mice were found in the milk of women in all 3 populations. B-type particles were found in 5% of milk samples from women with no familial history of breast cancer, in 60% of women with such a history and in 39% of Parsi women. Similarities between human and murine breast cancer, including the viral factor, the presence of family groups, appear to suggest that murine breast cancer is a valuable experimental model for human breast cancer.

1420 INFECTIVITY OF CELL CULTURES BY A VIRUS ISOLATED FROM A MAMMARY CARCINOMA OF A

RHESUS MONKEY. (E.) Chopra, H. C. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), I. Zell E. M. Jensen, M. M. Mason and N. J. Woodside. *J Cancer Inst* 46(1):127-137, 1971.

Propagation of a virus isolated from monkey mammary carcinoma was effected by cocultivation of the monkey embryo cells and tumor tissue. Virus particles

in the form of intracytoplasmic A-type particles and extracellular enveloped particles similar in appearance to those observed in the original tumor were isolated. Infected embryo cells revealed the presence of the intracytoplasmic particles one wk after virus inoculation with extracellular forms appearing at 10 days. Infected cells of monkey lung contained polyribosomes and rough endoplasmic reticulum. Chimpanzee lung cells which were infected were characterized by a well-developed endoplasmic reticulum and large numbers of mitochondria; intracytoplasmic A-type particles were seen in a few cells post-inoculation. Infected cultures of normal human leukocytes (NC37) showed typical blast cells, scanty endoplasmic reticulum, abundant free ribosomes, and a few mitochondria, whereas in human embryonic cell cultures the developmental pattern was identical to that seen in other cultures. In the absence of any apparent cytopathic changes, the visualization of intracytoplasmic A-type particles and their subsequent budding from the cell surface were the only criteria used to determine infectivity.

- 1421 OBSERVATIONS OF VIRUS IN VIRUS-INDUCED TUMORS IN HAMSTERS. (Fr.) Cesarini, J. P. (Reg. Anti-Cancer Ctr., Marseilles, France). *C R Acad Sci* 272(6):901-904, 1971.

The BHK 21/C 13 cells in culture as well as the clones obtained after transformation of these cells by oncogenic DNA and RNA virus contain a virus of a characteristic structure and development in their cytoplasm. This virus was not found in the *in vivo* virus-induced tumors in animals reared under the conditions described in this study. Systematic examination by means of electron microscopy was conducted in over 5000 healthy animals and in those with tumors induced by polyoma virus or by the injection of transformed cells. Subcultures of BHK 21/13, during its maintenance in culture, revealed the presence of a virus (H) with a central nucleoid and a clear center. The virus had a distinct topography and was present in the cell cytoplasm and in cisterns and dilated vacuoles. The H virus was found at times in association with C particles in inter- or intra-mitochondrial (RB 12) sites or with mycoplasma (CL 2 TSV 5). It was found in all strains of cultures whose origin was the BHK 21/13, and also in the tumors produced by injection of such strains, but was not found in the tumors which were originally induced by the polyoma virus (CT 54, CT 55). A similar viral structure has been described in cultures of calf kidneys.

- 1422 DISTRIBUTION OF INTRACISTERNAL A-PARTICLES IN A VARIETY OF NORMAL AND NEOPLASTIC MOUSE TISSUES. (E.) Wivel, N. A. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.) and G. H. Smith. *Int J Cancer* 7(1):167-175, 1971.

Neoplastic and non-neoplastic mouse tissues were examined by electron microscopy for the presence of intracisternal A particles. Non-neoplastic tissues harboring A-particles included the ectoderm of mammary glands and the mesoderm of seminal vesicles, ovaries and spleen. Malignant tissues containing

A-particles included the ectoderm of mammary adenocarcinomas, the mesoderm of plasmacytomas and Leydig cell tumors, and the endoderm of pulmonary adenomas, hemangioendotheliomas and hepatomas. A-particles usually measured 75-85 m μ in diameter, although some of the tumor cell particles were larger. The presence of particles in gonadal tissue of both sexes appeared to suggest that the particles may be transmitted vertically. It was noted that A-particles were found in most of the tissues known to support the replication of mouse leukemia and mammary tumor viruses. A-particles were seen to co-exist with viral C-type particles and with intracytoplasmic A-particles. Intracisternal A-particles may represent a marker for incomplete viral replication, representing the partial gene expression of an oncogenic RNA virus.

- 1423 AN UNUSUAL VIRUS IN CULTURES FROM A HUMAN NASOPHARYNGEAL CARCINOMA. (E.) Achong, B. G. (U. Bristol Med. Sch., England), P. W. A. Mansell, M. A. Epstein and P. Clifford. *J Nat Cancer Inst* 46(2):299-307, 1971.

Virus particles were found in cultured lymphoblastoid cells derived from a nasopharyngeal carcinoma from a Kenyan African. The tumor cell monolayer culture released the virus-bearing lymphoblastoid cells after 105 days in culture; 10% of the intact cells contained particles. Virus particles appeared in immature and mature forms. The immature form of particle was spherical, about 45 m μ in diameter, and had an electron-opaque outer zone and an electron-lucent center. These particles were present only in cytoplasm and passed through cell membranes by budding. The mature virus consisted of the immature spherical center surrounded by evenly spaced spines radiating from its surface. The overall diameter of the particle from spine tips was 110 m μ . Where cells were juxtaposed, the virus produced a thickening of the cell plasmalemma and a development of spines at the sites of viral budding. Although these virus particles could not be classified decisively, they were similar to feline fibrosarcoma virus and bovine lymphosarcoma virus, and had some of the features of the mouse mammary tumor agent.

- 1424 *IN VITRO* STUDIES OF RAT VIRUSES: II. EFFECTS OF HEAT, X-IRRADIATION AND CARCINOGENIC DRUGS. (E.) Lum, G. S. (VA Hosp., Cincinnati, Ohio). *Oncology* 24(6):416-430, 1970.

Incubation of rat viruses (strains L-S and RV) in rat embryo cell cultures at 42° produced lower virus titers than incubation at 37° by 0.75-1.0 logs; the depression of virus titer with high temperature was general; however, at day 6 of incubation L-S strain virus-infected cells were 0.5 log titers higher in cultures incubated at 42° than in cultures incubated at 37°. Incubation of cells at 42° produced virus 1 day later than incubation at 37°. Treatment of cultures with D₂O enhanced virus titers in cells incubated at 42°, producing a 3 log increase on day 3 of incubation. Exposure of virus-infected cells to 480 rads of X-irradiation delayed the cytopathic effect, but did not reduce virus titers; a decrease in virus

titers of 1.5 logs resulted from exposure to 800 rads. Virus-infected cells treated with 3-methylcholanthrene produced virus 135 days after treatment, while untreated cells infected with virus did not produce virus; treatment with 2-aminobiphenyl did not result in the emission of virus by infected cells. Increasing doses of benzo(a)pyrene caused cells to emit virus after decreasing period. Twelve and 8 μ g caused the virus-production cycle to begin after 7 and 8 days, resp.; 4 μ g caused the cycle to begin at 14 days. Urethan, methylbenzo(a)pyrene, cadmium sulfide and cadmium oxide also increased the amount of virus produced by infected cells. Mustargen did not affect the cycle of virus production, and thioTEPA decreased the amount of virus produced.

- 1425 HISTOLOGIC AND ELECTRON MICROSCOPIC OBSERVATIONS ON A TUMOR-BEARING VIPER: ESTABLISHMENT OF A "C"-TYPE VIRUS-PRODUCING CELL LINE. (E.) Zeigel, R. F. (Roswell Park Mem. Inst., Buffalo, N. Y.) and H. F. Clark. *J Nat Cancer Inst* 46(2): 309-321, 1971.

An edematous myxofibroma weighing 117.5 g was found in the precardial area of an adult female Russell's viper (*Vipera russelli*). Although no virus particles could be found in suspensions of tumor tissue, the morphology of the tumor cells was similar to those of a cell line (VSW) derived from the spleen of this tumor-bearing Russell's viper; this cell line has yielded viral C-type particles. The tumor was composed of sheets and cords of intensely-staining cells similar both to fibroblasts and to epithelial cells. Metastatic intravascular cells were found in spleen, kidney, liver and pancreas. Both primary and metastatic cells had desmosomes, tonofibrils, and large nuclei. Clusters of strongly basophilic cells in the venous lumina were also seen. The VSW cell line appears to have originated from tumor metastasis to the spleen.

- 1426 NEW CALIBRATION CORRELATIONS FOR MOLECULAR WEIGHTS OF CIRCULAR DNA: THE MOLECULAR WEIGHT OF THE DNA OF AN ONCOGENIC PAPOVA VIRUS OF THE SYRIAN HAMSTER. (E.) Bottger, M. (German Acad. Sci., Berlin, Germany), D. Bierwolf, V. Wunderlich and A. Graffi. *Biochim Biophys Acta* 232(1):21-31, 1971.

Interdependence between the sedimentation coefficient and molecular wt was studied through sedimentation analysis of the DNA of a Syrian hamster papova virus. Derivation of two equations for the closed ring form and for the open relaxed ring component II, $s_{11}^0 - 5.16 = 0.00439 M^{0.553}$ and $s_{11}^0 - 2.50 = 0.219 M^{.435}$, gave determinations of molecular wt which were 10-15% lower than values calculated according to other equations in use, showing an average of $3.1 \cdot 10^6$ which coincides closely with the molecular wt of $3.3 \cdot 10^6$ determined by electron microscopy. Two homogeneous DNA components were observed in addition to heterogeneously sedimenting material with sedimentation coefficients < 12 S; relative proportions showed the predominant heterogeneous component to be Component II, the open-relaxed ring component. The relation

of the expansion parameters in linear and circular DNA $e_{11}^0 = e_C^0$ is justified on the basis of present findings.

- 1427 HUMAN SARCOMAS IN CULTURE: FOCI OF ALTERED CELLS AND A COMMON ANTIGEN; INDUCTION OF FOCI AND ANTIGEN IN HUMAN FIBROBLAST CULTURES BY FILTRATES. (E) Giraldo, G. (Sloan Kettering Inst. Cancer Res., New York, N.Y.), E. Beth, Y. Hirshaut, T. Aoki, L. J. Old, E. A. Boyse and H. C. Chopra. *J Exp Med* 133(3):454-478, 1971.

Primary cultures of human osteosarcomas, leiomyosarcomas and fibrosarcomas were composed primarily of fibroblasts; these became more predominant in successive passages. Human sarcoma cultures usually started to proliferate after 4-6 wk in culture. Three of 7 cultured sarcomas developed into colonies of altered cells after 4-5 months in culture, and consisted of foci of randomly oriented crisscrossing cells. In some sarcoma lines, foci disappeared for periods of time and then reappeared; the appearance of foci at a particular time in a particular sarcoma culture was found to be characteristic of that sarcoma. In 12 of 23 attempts, foci were produced in human fibroblast cultures by filtered medium of sarcoma cultures within 1-2 wk from the time of introduction of the filtrate; no foci appeared in fibroblasts not exposed to filtrates. Induced foci were morphologically and ultrastructurally similar to spontaneous foci arising in sarcoma cultures. Electron microscopy failed to reveal evidence of viruses present in sarcoma cultures or in foci. When sera from patients with osteosarcoma were tested by indirect immunofluorescence for reaction with 7 sarcoma lines, positive reactions were elicited with 6 of these lines. Immunofluorescence also revealed a surface antigen in the cytoplasm of 12 of 15 sarcoma cultures; primary culture of sarcoma cells did not demonstrate surface antigen. No relationship was found between focus formation and antigenicity in sarcomas, or between the ability of sarcoma filtrates to induce foci in fibroblasts and antigenicity. Filtrates from 3-day-old sarcoma cultures induced the appearance of antigen in 0.01-1% of human fibroblasts.

- 1428 C-TYPE VIRUS PARTICLES IN PIG KIDNEY CELL LINES. (E.) Armstrong, J. A. (Natl. Inst. Med. Res., London, England), J. S. Porterfield and A. T. De Madrid. *J Gen Virol* 10(2):195-198, 1971.

A non-cytopathic virus morphologically similar to the oncogenic C-type virus particles was examined in pig kidney cells by electron microscopy. Extracellular rounded virus particles were found in the vicinity of 25% of cells; the particles measured 95-115 nm in diameter. The C-type particles were more common in the PS, PK15 and IB-RS-2 cultures of pig kidney cells than in SK6 cells. The particles consisted of an envelope separated by a zone of low density from a core of high density; the core was irregular in outline and often showed a fibrillar substructure. The core measured 60-85 nm in diameter. Particles budding off

ward from the cell surfaces were frequent. The significance of the observation of C-type virus particles in pig kidney cells, and the mode of their introduction into these cells, is obscure.

1429 PURIFICATION OF THYMIDINE KINASE ACTIVITY FROM YABA VIRUS INDUCED TUMORS. (E.)

Gordon, H. L. (Roswell Park Mem. Inst., Buffalo, N. Y.). *J Med* 1(2):110-116, 1970.

Cell-free extracts of monkey tumors induced by Yaba pox virus were subjected to acetic acid and ammonium sulfate precipitation in order to isolate the thymidine kinase of the tumors in a pure form. The precipitated enzyme was subsequently purified by DEAE-cellulose column chromatography. A 1.4-fold increase in activity was found in the acetic acid-precipitated fraction; precipitation of this fraction with 30% (NH₄)₂SO₄ resulted in a 2.5-fold increase in activity. Three protein fractions were separated on column chromatography, which showed thymidine kinase activity 102-fold, 100-fold and 45-fold greater than the activity-levels of the original reaction mixture.

1430 BIOPHYSICAL CHARACTERIZATION OF THE YABA TUMOR POX VIRUS. (E.) Fiel, R. J. (Roswell Park Mem. Inst., Buffalo, N. Y.), H. L. Gordon and R. F. Zeigel. *J Med Exp Clin* 1(3):142-155, 1970.

Yaba tumors were induced on the backs of stump-tailed Macaque and rhesus monkeys by s.c. inoculation of tumor homogenates; tumors were excised after 4 wk of growth, and the Yaba pox virus was isolated, purified and characterized by rate and isopycnic zone centrifugation, electron microscopy and small- and wide-angle light scattering methods. A single rate zonal centrifugation treatment eliminated 85-90% of total tumor protein without loss of virus. Isopycnic banding of the rate zonal fractions allowed isolation of 4 virus particles, designated L, M, N, and X. The banding density of particle L was 1.11, while that of M and N was 1.26; no banding density for X was recorded. Light scattering experiments indicated that particles L, M, and X all measured about 400 nm in diameter, while particle N measured about 500 nm. L particles were thought to be immature virions, while M particles were considered to be mature. N particles appeared to consist of aggregates of M particles. The nature and composition of the X particles remained unclear.

1431 RNA DEPENDENT DNA SYNTHESIS IN CELL FREE PREPARATIONS OF HUMAN LEUKEMIA CELLS. (E.)

Ackermann, W. W. (Dept. Epidem., U. Michigan, Ann Arbor), W. H. Murphy, B. A. Miller, H. Kurtz and S. T. Barker. *Biochem Biophys Res Commun* 42(4):723-729, 1970.

To test the possibility that human leukemia has a viral etiology, a continuous line of cells established from a case of human leukemia was selected and examined for RNA primed DNA polymerase activity. Incorporation of H³-thymidine phosphate into acid-insoluble material could be shown to be approximately

a linear function of the concentration of the enzyme with dilutions greater than 30% and was absolutely dependent upon the presence of MgCl₂, all 4 deoxy-ribonucleotide triphosphates and enzyme. Incorporation was reduced 78-83% by RNase treatment but was not markedly affected by a nonionic detergent or lysozyme; however, it was almost completely inactivated by trypsin. The acid-insoluble product into which ³H-thymidine phosphate was incorporated had the properties of DNA. The enzyme activity obtained from these cells is not distinctly different from that reported in tumorigenic virions, but there is no evidence that the active particle is a virion.

1432 INCIDENCE OF EB VIRUS-CONTAINING CELLS IN PRIMARY AND SECONDARY CLONES OF SEVERAL BURKITT LYMPHOMA CELL LINES. (E.) Maurer, B. A.

(Roswell Park Mem. Inst., Buffalo, N. Y.), T. Imamura and S. M. Wilbert. *Cancer Res* 30(12):2870-2875, 1970.

Burkitt lymphoma cell lines cloned by agar droplet and single-cell isolation procedures were examined for the presence of Epstein-Barr virus-containing cells by an indirect immunofluorescent antibody test. Of 10 parental cell lines tested using the agar droplet method, 6 were placed in a high-virus-incidence group and 4 in a low-virus-incidence group, separation being based upon whether the cell line had greater than or less than 1 fluorescent cell per thousand counted. Of 12 groups of clones produced from the high-incidence group, 8 were 100% positive. The range of Epstein-Barr virus positiveness for each group of clones was usually broader and lower than that of the parental culture with incorporation of 7S globulin showing no effect on incidence or range of positiveness. In the low-incidence group, when clones were established, all cultures produced at least 1 positive clone, with proportion of positive cells being equal to or greater than the parental culture; incorporation of 7S globulin had no effect on the incidence or range of positiveness. In clones derived from single Burkitt lymphoma cells, 6 cell lines were selected; 3 had an incidence of positive cells of greater than 1 cell per thousand and 3 showed negativity by indirect immunofluorescent testing. All single cell clones in the high-incidence group were virus positive and the range of positivity of derived clones was broader and lower than the range of parental cultures. The incidence of virus-positive clones derived from the low-incidence parental group of cultures by single-cell isolation was 8.5% and by the agar droplet method, 7.1%. Cloning efficiency for the single-cell isolation procedure ranged from 2 to 22% and no correlation between cloning efficiency and incidence of Epstein-Barr virus-containing cells was noted. A genetic potential for virus synthesis which is vertically transmitted from parent to daughter cell in the Burkitt cell lines studied is indicated from these studies.

1433 SOME BIOPHYSICAL ASPECTS OF E-B VIRUS ADSORPTION TO THE SURFACES OF THREE TYPES OF MAMMALIAN CELLS. (E.) Weiss, L. (Roswell Park Mem. Inst., Buffalo, N. Y.) and S. J. Horoszewicz. *Int J Cancer* 7(1):149-159, 1971.

Virus adsorption in human peripheral normal, leukemic and myelomatous blood cells with respect to electrokinetic properties of the cell surfaces was studied by immuno-fluorescent and electron microscopic techniques. Both RNase and neuraminidase produced significant reductions in cell surface net negativity, and the combination of the enzymes resulted in greater reductions than either one when used singly; a sharp diminution in the mean mobility of one type of virus-adsorbing cells was seen as calcium concentrations were altered. In non-adsorbing cells, the mean rate of decrease in surface negativity was highest as the concentration of environmental calcium increased, and in the virus-adsorbing cells, the mean rate of decrease was less marked. Treatment of the cells and virus suspensions with enzymes and varying calcium ion concentrations did not demonstrably change the pattern of cell-virus interaction compared to untreated controls. Electron microscopic examination revealed virus particles attached to 2 cell lines previously recognized to adsorb viruses in contrast to the absence of particles in the non-absorbing cell line used here, which was taken from a patient with multiple myeloma.

- 1434 ELEVATED ANTIBODY TITERS TO EPSTEIN-BARR VIRUS IN HODGKIN'S DISEASE. (E.) Levine, P. H. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), D. V. Ablashi, C. W. Berard, P. P. Carbone, D. E. Waggoner and L. Malan. *Cancer* 27(2): 416-421, 1971.

Indirect immunofluorescence tests were performed on sera from patients with Hodgkin's disease, normal controls, patients with non-malignant disease, and patients with lymphomas other than Hodgkin's disease, and the Epstein-Barr virus (EBV) antibody titers recorded from these groups were compared. Thirty-four percent of Hodgkin's disease patients had EBV antibody titers in excess of 1:640, while 11.9% of "other lymphoma" patients, 3.5% of non-malignant condition patients, and 4.7% of normal subjects had titers at this level. Geometric mean titers of EBV antibody for these 4 groups were 1:367 (Hodgkin's disease), 1:132 (other lymphoma), 1:162 (non-malignant pathology), and 1:91 (normal subjects). Patients with the mixed cellularity form of Hodgkin's disease had the highest geometric mean titers of antibody (1:736), and those with the nodular sclerosis type of Hodgkin's disease had the lowest geometric mean titers (1:177). Patients with high titers of EBV antibody generally had had symptoms of Hodgkin's disease for longer periods, were in more advanced stages of the disease, survived for shorter periods, and showed more lymphocyte depletion, than patients with low titers. Treated patients had higher titers than untreated patients. No differences were found between Hodgkin's disease patients and normal subjects in the titers of antibody to herpes simplex viruses types I and II, cytomegalovirus, or varicella. The findings did not indicate whether EBV has an etiological role in Hodgkin's disease as opposed to the role of a passenger virus ancillary to the genesis of the condition.

- 1435 FURTHER CHARACTERIZATION OF THE WI-L1 AND WI-L2 LYMPHOBLASTOID LINES. (E.) Levy, J. A. (San Francisco Med. Ctr., Calif.), D. N. Buell, C. Creech, Y. Hirshaut and H. Silverberg. *J Nat Cancer Inst* 46(3):647-654, 1971.

Attempts to isolate virus by inoculating cell free extracts of cells from 2 human lymphoblastoid cell lines onto monolayer cultures proved fruitless. The lymphoblastoid cell lines, designated WI-L1 and WI-L2, were originally derived from 2 patients, 1 with mycosis fungoides and 1 with hereditary spherocytic anemia. Although fluorescence studies had indicated that Epstein-Barr virus was present in line WI-L1, the virus could no longer be demonstrated after the line had been in culture for 6 months. Antibodies to Epstein-Barr virus were demonstrated in both cell lines and in all the members of the family of the donor of cell line WI-L2. Both cell lines were found to synthesize IgG-type molecules, and both had similar rates of IgG synthesis; IgG counts rose steadily from zero to 8,000 over 60 min in culture with ³H-leucine. A subline of cells from WI-L1 with a unique #1 chromosome having a subterminal secondary constriction was established.

- 1436 TRANSFORMATION AND DIFFERENTIATION OF RENAL TISSUE INDUCED BY A RNA VIRUS. (Fr.) Lacour, F. (Inst. Gustave Roussy, Villejuif, France), O. Weiler, R. Gerard-Marchant and E. Delain. *Bull Cancer* 57(3):335-344, 1970.

An avian myeloblastoma line was established in Leghorn chicks in renal tissue (DNV). The chicks were inoculated with an acellular extract corresponding to 0.3 g of tumor tissue and 3 successive transmissions were possible by the same technique. Examination by electron microscopy showed the presence of viral particles comparable to the avian myeloblastosis virus (AMV) of the primary tumor. The intrarenal tumor proliferation shows a predominance of blastomas with complex differentiation, both epithelial and mesenchymal. The virus exhibited a particular tropism for renal tissue. Although inoculated into a highly sensitive strain at an age most sensitive to leukemogenic virus, the virus appeared in renal tumors in 94% of the cases, and no leukemia or other malignant neoplasm was observed. The virus induces a malignant transformation of nephrogenic cells which then undergo all the types of cell differentiation from nephron alone to various connective tissue, bone or hemopoietic tissue.

- 1437 HETEROGENEITY OF STRAIN R AVIAN (ERYTHROBLASTOSIS) VIRUS. (E.) Ishizaki, R. (Duke U. Med. Ctr., Durham, N. C.) and T. Shimizu. *Cancer Res* 30(12):2827-2831, 1970.

Avian erythroblastosis virus strain R (AEV-R), an agent which produces erythroblastic leukemia in chickens, had an LD₅₀ of 10^{-4.5} ml of a 10% liver homogenate from leukemic birds of the 4th passage. Inoculated chickens responded by antibody or viremia

production to dilutions higher than those causing frank leukemia. Tests were performed to investigate the interference resistance of AEV-R against Rous-associated virus in chick embryo cells; interference was produced by a 10^{-6} dilution of virus in liver homogenate. Chick embryo cells were transformed by AEV-R in dilutions of 10^{-4} ; AEV-R foci were noted following inoculation of the chick embryo cells with 10^{-1} dilutions of virus. While the infectious capacity for chickens of AEV-R as measured by viremia and antibody production was 1000-fold greater than the capacity for leukemogenic activity, the virus' ability to infect chick embryo cells measured by interference was 10-fold less than its ability to induce leukemia in chickens. Passage of AEV-R in tissue culture reduced leukemogenic activity. AEV-R was neutralized by anti-Rous associated virus antiserum, suggesting that AEV-R is a member of virus subgroup B of avian tumor viruses. A component of AEV-R derived directly from chickens was found to infect but not to transform chick embryo cells, suggesting that AEV-R is heterogeneous.

1438 COMMON SEQUENCES BETWEEN RNA FROM ONCOGENIC VIRUSES AND CELLULAR DNA. (Fr.)

Harel, J. (Inst. Gustave Roussy, Villejuif, France), L. Harel and G. Frezouls. *Bull Cancer* 57(3):283-300, 1970.

Competitive hybridization experiments showed that only one fraction of RNA 65 S of avian myeloblastosis virus (AMV) can be hybridized at a high concentration with cellular DNA, and that this fraction of the viral RNA must be identical or quasi-identical with certain sequences of RNA normally transcribed in the non-infected cells of the chick. These results obtained after partial recurrent hydrolysis of RNA 65 S of AMV demonstrated that only a small fraction of cellular RNA, probably bound to cytoplasmic membranes, contained sequences identical with the hybridizable viral RNA sequence. These sequences were present in similar quantities in the intact as well as the virus-infected cells transformed by AMV; the same doses of cellular RNA of normal liver or myeloblasts inhibit almost completely the hybridization of RNA 65 S with the DNA of cells producing the virus. It is possible to envision from the results that the common sequences between the viral RNA and cellular DNA represent sites of attachment for future integration of the viral genome in the cellular genome.

1439 AN AVIAN LEUKOSIS VIRUS RELATED TO RSV(O): PROPERTIES AND EVIDENCE FOR HELPER ACTIVITY. (E.) Vogt, P. K. (U. Washington Sch. Med., Seattle) and R. R. Friis. *Virology* 43(1):223-234, 1971.

Inoculation of type C/A chick fibroblasts and Japanese quail fibroblasts with Rous sarcoma virus type O [RSV(O)] produced infectious progeny virus in 1.35% of Japanese quail cells and in 78% of chicken cells. The efficiency of virus-production among RSV(O) colonies in quail cells increased with increasing multiplicity of infection; undiluted virus inocula produced RSV(O) in 73% of cases, while virus

dilutions of 1:50 produced virus in 8.5% of cases. Apparently, the virus-producing colonies in chicken cells contained a helper agent which facilitated the reproduction of RSV(O); this agent could be transferred to quail cells. Treatment of quail fibroblasts with sonically disrupted transformed chicken cells enabled quail cells to produce virus in 100% of the fowl. The transmissible agent discovered in chicken cells was found to have all the attributes of an avian RNA leukosis virus with envelope antigens identical to those of RSV(O). The agent was designated Rous-associated virus type O [RAV(O)]. Quail cells were found to lack the group-specific antigen of the avian leukosis virus, while all chicken cells did harbor this antigen. RAV(O) apparently plays an essential role in the replication of RSV(O) in group-specific antigen-negative cells such as Japanese quail fibroblasts. RAV(O) did not interfere significantly with the plating efficiency of RSV(O) when cultures were co-infected with the 2 viruses. RAV(O) did not infect quail cells when inoculated alone in the absence of RSV(O).

1440 ISOLATION OF THE NUCLEIC ACID OF FELINE LEUKEMIA VIRUS. (E.) Jarrett, O. (Dept.

Biochem., U. Glasgow, Scotland), J. D. Pitts, J. M. Whalley, A. E. Clason and J. Hay. *Virology* 43(1):317-320, 1971.

RNA isolated from cultures of feline leukemia virus (FeLV) was found to be similar to RNA of the avian and murine leukemia viruses. The FeLV used was isolated from a cat with spontaneous alimentary lymphosarcoma and was grown in feline embryonic cells. The viral RNA was extracted by the SDS-phenol method and by the SDS-pronase method. The viral RNA separated on Sephadex G-100 columns into 2 components, 1 of which was excluded from the gel and appeared in the void volume and 1 of which eluted with the 4S marker cellular RNA. The former RNA showed a major 75S peak on sucrose gradient centrifugation. These 2 major components of the FeLV virus RNA are similar to those from other RNA tumor viruses.

1441 CURRENT INFORMATION ON FELINE AND CANINE CANCERS AND RELATIONSHIP OR LACK OF RELATIONSHIP TO HUMAN CANCER. (E.) Gardner, M. B. (U. Southern Cal. Sch. Med., Los Angeles). *J Nat Cancer Inst* 46(2):281-290, 1971.

In a study of 103 domestic cats, C-type feline tumor virus was found in 70% of cats with lymphoma, 20% of cats with sarcoma, and in 20% of cats with carcinoma. Virus has also been found in livers of fetal cats at 3-7 wk gestation. The feline virus has been isolated from a spontaneous feline fibrosarcoma and its inoculation has produced sarcomas in monkeys, kittens, puppies and rabbits. In tissue culture studies, feline, canine and human embryo cells were found to be susceptible to transformation by feline virus; viral particles were released from transformed cultures. Human tumors were transmissible to fetal cats using cloned human sarcoma cells which were either infected or uninfected with feline virus. No causal relationship has been found between virus-

associated cancers of cats and human or canine cancers; cats apparently do not spread feline virus to dogs or to men. The virus is probably inherited among cats but it may be transmitted in bites or scratches.

- 1442 INTRACISTERNAL VIRAL PARTICLES IN MURINE LEUKEMIAS. (E.) Braylan, R. C. (Nat'l. Acad. Med., Buenos Aires, Argentina), L. Z. De Tkaczewski, M. E. M. Colmerauer and C. Dosne Pasqualini. *Medicine* 30(5):459-464, 1970.

Leukemia was induced in inbred mice by intrasplenic injections of allogenic leukemia cells, by syngeneic leukemia cells administered in subthreshold s.c. doses, or by i.p. injections of acellular supernatants of homogenized leukemic tissues. These leukemias killed host mice by 70 days postinoculation and were diagnosed as lymphoblastic leukemias characterized by massive infiltration of poorly differentiated lymphoblasts. Under the electron microscope, leukemia cells from mesenteric lymph nodes and s.c. leukemic infiltrations showed intracisternal A type virus particles and, rarely, A particles were seen budding from cellular membranes. Particles seen in the cisternae measured about 70 nm in diameter, were spherical, and showed varying electron density. The particles apparently emerged from thickenings of the rough endoplasmic reticulum. The association of intracisternal A particles with A and C particles in and around the same cell was striking. Intracisternal A particles may be as important in the mechanism of leukemogenesis as the classic A and C particles.

- 1443 EARLY MORPHOLOGICAL CHANGES ASSOCIATED WITH INFECTION BY A MURINE NONTHYMIC LYMPHATIC TUMOR VIRUS. (E.) Rabstein, L. S. (Microbiol. Ass., Walkersville, Md.), A. F. Gazdar, H. C. Chopra and H. T. Abelson. *J Nat Cancer Inst* 46(3):481-491, 1971.

One-day-old mice given i.p. inoculations with 1.5 infectious U of a strain of Moloney leukemia virus (MLV-A) developed solid lymphatic tumors which became noticeable by 12 days after inoculation of virus, and which left only 2 of 90 mice alive at 26 days post-inoculation. The spleen wt in the inoculated group increased significantly compared to that in uninoculated groups. Tumors began to appear on the meninges on day 14; the earliest evidence of tumor infiltration within the spinal cord coverings was seen microscopically on day 18. Visible and palpable nodes were first noted on day 18; they grew rapidly thereafter, with tumors appearing first in the cortical area. Preneoplastic changes in lymph node tissue included abundant polymorphonuclear leukocytes and pyknotic lymphocytic nuclei. Grossly enlarged spleens were evident on day 14, and myelotic cell precursors began to increase in bone marrow on day 12. Tumors consisted chiefly of lymphoblasts which grew rapidly in all cases and were markedly invasive. There were no signs of leukemic development in the blood of infected animals, and neither kidney, liver, nor adrenal glands were involved. Budding type-C virus par-

ticles were seen in tumor tissue and in nontumorous tissue in the spleen, marrow, thymus and dura.

- 1444 STREPTOVARICINS INHIBIT RNA DEPENDENT DNA POLYMERASE PRESENT IN AN ONCOGENIC RNA VIRUS. (E.) Brockman, W. W. (Johns Hopkins U. Sch. Med., Baltimore, Md.), W. A. Carter, L. H. Li, F. Reusser and F. R. Nichol. *Nature* 230(5291):249-250, 1971.

Reaction mixtures containing Moloney strain murine leukemia virus and streptovaricins in amounts ranging from 20-400 µg/ml significantly inhibited the RNA dependent DNA polymerase activity in the virus. A streptovaricin complex containing 7 macrolides as well as undetermined components produced 77% inhibition at 40 µg/ml doses; increase of the streptovaricin dose to 100 and 400 µg/ml gave inhibitions of 77% and 68%, resp. Streptovaricin C resulted in a 73% inhibition of RNA dependent DNA polymerase at 400 µg/ml, and streptovaricin A produced 33% inhibition at the same dose. Streptolydigin and rifampicin caused 3 and 13% inhibition, resp., while rifamycin SV inhibited polymerase activity 77% at 400 µg/ml.

- 1445 SENSITIVITY OF JLSV-9 CELLS TO MOLONEY LEUKEMIA VIRUS IN RELATION TO CELL CYCLE. (E.) Gergely, L. (Karolinska Inst., Stockholm, Sweden), M. Cikes, E. Klein, E. M. Fenyö and S. Friberg. *Exp Cell Res* 64(1):230-232, 1971.

Infection parameters, including mitotic index, modal cell volume, ³H-thymidine incorporation, and membran antigen appearance were investigated in synchronized cell cultures of JLSV-9 cells inoculated with Moloney leukemia virus (obtained from a YAC ascites lymphoma). Cell cultures were inoculated with 1 ml of a 1:100 dilution of the virus. The mitotic index of the infected cells dropped sharply from 0.95 to 0.10 by 1 hr after colcemid release of the synchronized cell, and thereafter remained at or near the lower level. Modal cell volume also dropped abruptly between 0-5 hr after colcemid release, decreasing by a factor of 2, and recovered by 13 hr after colcemid release, returning to near initial values. Tritiated thymidine increased precipitately following colcemid release, values rising from 2.0 cpm x 10³ at 0 hr to 20 cpm at 6 hr; thereafter, ³H-thymidine incorporation declined to 3.0 cpm at 15 hr after colcemid release. Antigen positive cells began to appear in cultures at day 18 after the initiation of cultures. Culture infected with virus 2-5 hr after metaphase arrest had higher antigenicity than other cultures. By day 35 the different cell cultures had similar proportions of membrane antigens.

- 1446 FORMS OF DEOXYRIBONUCLEIC ACID PRODUCED BY VIRIONS OF THE RIBONUCLEIC ACID TUMOR VIRUSES. (E.) Manly, K. F. (Massachusetts Inst. Technol., Cambridge), D. F. Smoler, E. Bromfeld and D. Baltimore. *J Virol* 7(1):106-111, 1971.

Sucrose gradient sedimentation of the DNA produced by DNA polymerase in murine leukemia viruses (Moloney

strain) showed that the DNA product consisted of 2 fractions: one fraction sedimented at the same rate as native viral RNA (60-70S) and was called the fast fraction; the other fraction sedimented at less than 15S (the slow fraction). The fast fraction contained most of the DNA product after 20 min of reaction; by 120 min of the reaction the slow fraction contained most of the DNA product. Enzyme analysis with enzymes of known specificity showed that the slow fraction from a 120 min reaction consisted of 50% single-stranded DNA and 40% double-stranded DNA, and of 10% hybrid DNA; after a 20 min reaction the slow fraction consisted of 70% single-stranded DNA, 15% hybrid DNA, and 15% double-stranded DNA. After a 120 min reaction the fast fraction consisted of 40% single-stranded DNA, 35% hybrid DNA, and 25% double-stranded DNA. After a 20 min reaction, the fast fraction consisted of 45% single-stranded DNA, 45% hybrid DNA, and 10% double-stranded DNA. Findings of the relative proportions of single-stranded, hybrid and double-stranded DNA were confirmed by analysis on CS_2SO_4 gradients. In the presence of actinomycin D, the predominant DNA product was single-stranded. The variation in type of DNA produced by the virions may be accounted for by a model involving the successive displacement of single-stranded DNA as it is produced by double-stranded DNA; this conversion of single- to double-stranded DNA, according to the model, is obstructed by actinomycin D.

1447 RELEASE OF C-TYPE PARTICLES FROM NORMAL RAT THYMUS CULTURES AND THOSE INFECTED WITH MOLONEY LEUKEMIA VIRUS. (E.) Teitz, Y. (Israel Inst. Biol. Res., Ness-Ziona), E. H. Lennette, L. S. Oshiro and N. E. Cremer. *J Nat Cancer Inst* 46(1):11-23, 1971.

The amount of Moloney leukemia virus particles released into the media of rat thymus cell cultures was studied through determination of uridine- 3H incorporation into virus particles purified from the culture medium. Differences in radioactivity as high as 20-fold were seen in sucrose gradient fractions (density 1.16-1.18 g/ml) obtained from 100 ml of culture fluids, and no great differences in the rate of incorporation of uridine- 3H and thymidine- 3H into the RNA and DNA of the cells were noted. Cultures chronically infected with the leukemia virus incorporated uridine- 3H into cellular RNA at a linear rate for 6-8 hr. A 6-hr exposure to 0.5 μg actinomycin D/ml resulted in 96% inhibition in uridine- 3H incorporation, 0.2 μg /ml in 90% inhibition and 0.1 μg /ml in 50% inhibition, while 0.05 μg /ml caused no inhibition; cytosine arabinoside (10 μg /ml) or 5-fluorodeoxyuridine (100 μg /ml) produced no inhibition. Noninfectious C-type particles were isolated from control cultures which were not specifically precipitated with anti-Moloney leukemic virus serum. Sensitivity to actinomycin D action seems to characterize all members of the avian and murine leukemia groups, possibly indicating the requirement for cell-specific RNA synthesis at some stage of viral maturation.

1448 RAUSCHER VIRUS-INDUCED LEUKAEMIA IN MICE: THE ROLE OF 7 S AND 19 S ANTIBODIES IN THE STIMULATION OR INHIBITION OF THE LEUKAEMOGENIC

PROCESS. (Rus.) Ter-Grigorov, V. S. (P. A. Herzen Res. Inst. Oncol., Moscow, U.S.S.R.), B. I. Shevelev, O. Ya. Moskovkina and V. M. Bergolz. *Biull Eksp Biol Med* 71(1):61-64, 1971.

Immunological features of the 7 S and 19 S fractions of Rauscher virus (RV)-infected mouse serum were investigated. Two groups of C57BL/6 mice 1-1½-month-old were used: I) 50 mice were given i.v. 0.4 ml of plasma from leukemic BALB/c mice; II) 50 mice were given i.v. 0.2 ml of the same plasma at a 1:24 dilution (low dose). Twenty-five mice of each group were given complete Freund's adjuvant (FA) at this time. A third group (III) of BALB/c mice was given i.v. 0.3 ml of the RV-infected C57BL/6 mouse serum fractions (24 hr after infection) in order to determine its effects upon leukemogenesis. The 19 S antibodies comprised the first peak of immune response against the group specific antigen (GSA) in the low dose RV-treated mice 8 days after administration. Both the 19 S and 7 S fractions were found to be cytotoxic at the beginning stage of the next peak of immune activity against the type specific antigen (TSA) 26 days after the beginning of the experiment while later (40 days after viral infection) cytotoxicity was found to be determined by 7 S antibodies only. The low titer RV-infected mice exhibited an involutive pattern of leukemia. A minor early peak of immune activity due to 19 S antibodies and no other cytotoxic effects were seen in the high dose RV-infected mice; the cytotoxic effects of antibodies from the 19 S fraction directed against the GSA were blocked by the continuous presence of antibodies from the 7 S fraction. Most of these mice died of leukemia at the end of the 3rd month. Leukemogenesis in BALB/c mice (group III) was found to be stimulated by the 7 S fraction from the high dose RV-infected and by the 7 S serum fraction of the anti-GSA (first peak) of the low dose RV-infected mice; the 7 S fractions with peak anti-TSA activities had an inhibitory effect on the development of leukemic colonies in the spleen of the BALB/c mice. The immunological mechanism of the irreversible suppression by FA of the resistance against RV in the C57BL/6 mice seemed to be related to the stimulation of 7 S antibody formation against the GSA; these antibodies had high leukemogenic stimulating effects *in vivo*, and were able to block the cytotoxic effects of the 19 S antibodies *in vitro*.

1449 PREVENTION OF GROSS VIRUS-INDUCED LEUKEMIA IN PROGENY OF IMMUNIZED FEMALE RATS. (E.) Ioachim, H. L. (Lenox Hill Hosp., New York, N.Y.). *Cancer Res* 30(11):2661-2664, 1970.

The prevention of leukemia in the offspring of female rats immunized with Gross leukemia virus (GV) was investigated. Female rats from 3 strains were given a single i.p. injection of 0.5 ml of GV stock undiluted within 1 month before the first 2 wk of pregnancy; the number and interval of the doses was varied in some rats. The offspring of these treated rats were injected i.p. with leukemia-inducing doses of GV (0.1 ml of a 1/10 dilution of GV). Leukemia was prevented in offspring by maternal injection of GV in 100% of cases, while all control rats born from the mothers not

given GV died with thymoma and lymphoid leukemia 62-90 days after injection with GV. Average latency for development of leukemia in nonimmunized rats was 71-75 days. Four of 5 sera from immunized mothers gave a 4+ type-specific reaction in complement fixation tests with the AKR virus antigen; sera from the 2 nonimmunized mothers were negative in this test.

- 1450 EFFECTS ON FRIEND DISEASE OF DOUBLE-STRANDED RNA OF FUNGAL ORIGIN. (E.) Pilch, D. J. F. (Beecham Res. Lab., Betchworth, Surrey, England) and D. N. Planterose. *J Gen Virol* 10(2):155-166, 1971.

The effects on splenomegaly associated with Friend virus-induced leukemia of treatment with a double-stranded RNA obtained from a penicillium culture were investigated in mice infected with Friend virus. Male mice were given a single i.p. injection of double-stranded RNA (100 µg/mouse) at various times. Enhancement of splenomegaly followed injection of the fungal RNA when the injection was given between 5 days before to 3 days after infection of mice with virus. The mechanism of enhancement of splenomegaly was probably related to the immunosuppressive activity of the fungal RNA. Inhibition of splenomegaly followed injection of RNA when the RNA was injected 7-11 days after virus infection. This regression of splenomegaly was rapid; in 1 experiment inhibition of splenomegaly was noticed on day 14, and the RNA had been injected the day before. Inhibition of splenomegaly may have been related to interferon induction by the fungal RNA, or to a more specific antiviral or anti-tumor effect. In 1 group of mice given RNA on the 10th day after virus infection, the mice remained free of splenomegaly symptoms for some time, but by the 10th wk after RNA injections, 70% showed splenomegaly. Multiple injections of 50 µg RNA produced effects on splenomegaly similar to the effects produced by a single 100 µg injection. The spleens of mice in which splenomegaly was reduced by RNA injection had a normal structure.

- 1451 EFFECT OF 7,12-DIMETHYLBENZ(a)ANTHRACENE ON PHAGOCYTOSIS AND ANTIBODY FORMATION IN FRIEND VIRUS LEUKEMIA. (E.) Elliott, S. C. (Dept. Microbiol., U. Arizona, Tucson) and G. T. Schloss. *Infect Immun* 3(2):217-220, 1971.

Experiments were carried out to study the effect of 7,12-dimethylbenz(a)anthracene (DMBA) on phagocytosis and antibody formation in the spleen and on phagocytosis in the liver of BALB/c mice with Friend virus leukemia, utilizing carbon clearance and microtiter techniques. The phagocytic index K (measuring the carbon clearance of the entire animal) at 5 and 15 min was elevated in Friend virus-infected mice throughout the experiment; DMBA showed no significant effect on the phagocytic index of normal controls or infected animals. At 5 and 15 min, a progressive decrease of index α (measuring phagocytic activity/wt liver and spleen) was noted in infected animals. A significantly higher α was seen

in infected animals with DMBA. No real difference in carbon content in either spleen or liver at 5 or 15 min after injection was noted in controls and infected animals. In the normal spleen, dense columns of carbon-laden phagocytes surrounding the lymphocytic nodules were seen; in the normal liver Kupffer cells were found to contain large amounts of carbon. In the infected animals, when splenic architecture was destroyed, the number of carbon-containing phagocytes was small and no carbon was present in neoplastic cells of either liver or spleen. Serum hemolysin titers in infected animals were higher at the end of week 1, remained in the same range through weeks 2, 3 and 4, and became lower during weeks 5 and 6 when compared to controls. Treatment of infected animals with DMBA produced higher hemolysin titers than controls at the end of weeks 1, 2, 5 and 6 and titers within the same range as controls during weeks 3 and 4. Correlation of decreased carbon uptake by the spleen and decreased production of serum hemolysin would be possible only if the phagocytes which take up carbon were the same cells involved in the immune stimulus.

- 1452 ULTRAVIOLET INACTIVATION OF MURINE LEUKEMIA AND SARCOMA VIRUSES. (E.) Yoshikawa, H. (Fac. Sci. Orsay, France). *Int J Cancer* 7(1):131-140, 1971.

Friend leukemia viruses and murine sarcoma viruses were exposed to UV in order to investigate the sensitivity of these viruses to inactivation by UV; inactivation was assayed *in vitro* by the interference of UV-irradiated virus with focus-formation by murine sarcoma virus. For both viruses, the UV inactivation dose was 2,000-3,000 ergs/mm². The relative number of murine sarcoma virus foci/culture plate increased with increasing dilution of the preparation of irradiated Friend virus. The fraction of Friend virus surviving UV irradiation enlarged as the dose of UV administered decreased; at UV doses of 6,000 ergs/mm², the survival fraction was less than .01, while at UV doses of 2,000 ergs/mm², the survival fraction was about .1. It was found that murine sarcoma virus produced by cells incubated with 5-fluorouracil was more sensitive to UV-inactivation than control virus which were not incubated with 5-fluorouracil, a finding which may suggest that the viral nucleic acid was sensitized by the base analogue. Murine sarcoma virus which survive UV irradiation showed a prolonged latent period, possibly due to the interference of inactivated virions with the growth of surviving virions. In general, murine sarcoma virus inactivated by UV in the presence of excess Friend virus showed survival rates which were related to UV dose and were similar to survival rates of murine sarcoma virus inactivated by UV in the absence of Friend virus. When UV-irradiated murine sarcoma virus was titrated on the cells previously irradiated with UV, the slope of the inactivation curve was steeper than when the virus was titrated on the normal cells, suggesting that the UV-damaged viral genome may have been complemented by the corresponding homologous host genome.

453 INDUCTION AND REGRESSION OF FRIEND LEUKEMIA IN VACCINATED MICE BY MEANS OF PARABIOSIS. (E.) Takizawa, K. (Inst. Med. Sci., U. Tokyo, Japan) and T. Yamamoto. *Gann* 61(6):605-606, 1970.

Induction and regression of Friend leukemia virus-induced splenomegaly in hyperimmune DDD mice was studied by means of parabiosis. When splenomegalic mice were parabiotically united for 10 days with other DDD mice which had been vaccinated weekly 10 to 15 times with formalin-inactivated Friend virus preparation, splenomegaly was induced in the vaccinated mice. The parabionts killed on the 10th day had spleens similar in wt to the vaccinated and non-vaccinated animals (ranging from 1.62 to 2.25 g). Parabionts observed 1 month after separation from the non-vaccinated partners had spleens which had decreased to approximately normal wt (ranging from 0.25 to 0.45 g) and infectious Friend virus was not detected; non-vaccinated partners died within 20 days after separation. After 3 months, no evidence of a splenomegalic recurrence was found in the vaccinated survivors. Parabionts kept in union died within 50 days after joining. Prolongation of the parabiotic union from 10 days to 20 days resulted in a failure of the spleen to return to normal size in some of the vaccinated animals after separation, and splenomegaly continued until death. This model seems to be a useful means for analyzing induction and regression of leukemia when the primary focus is surgically removed.

454 FLUCTUATING VIRUS AND ENZYME LEVELS IN PLASMA OF MICE INFECTED WITH THE FRIEND LEUKEMIA VIRUS. (E.) Buscher, T. J. (Dept. Microbiol. Guelph, Ontario, Canada), C. Frantsi and K. F. Gregory. *Canad J. Microbiol* 17(3):315-321, 1971.

The nature and cause of the plasma enzyme fluctuations in Friend leukemia virus (FLV)-infected mice was studied in 8-wk-old female Connaught strain mice by various assay techniques. A strain of FLV, which was confirmed to be free of lactate dehydrogenase elevating virus (LDV) by comparison of the effects of FLV on plasma lactate dehydrogenase (LDH) with those of purified LDV, was used in these experiments. Pronounced fluctuation in plasma LDH in mice infected with FLV was seen as 3 dose-dependent peaks which were 20-20 times above the normal levels. The magnitude of the peaks varied from 2.0 to 44 IU/ml with a mean of 9.4 U/ml compared to the normal mean of 0.35 U/ml. Simultaneous infection of 5 mice with Friend leukemia virus and the LDH elevating virus resulted in 4-9-fold elevations in plasma LDH within 2-3 days with secondary rises noted 5-8 days post-infection giving peak titers of 5-16 U/ml (14 to 46-fold increase). The same degree of elevation occurred in mice inoculated with LDH elevating virus. Plasma virus titers compared closely with plasma enzyme levels; mice were shown to produce interferon in response to infection with the LDH elevating virus of about 40 U/ml at 20 hr post-inoculation. The possibility that interferon at levels below the sensitivities of the assay systems could be has not been excluded. Isocitrate dehydrogenase, aldol-

ase and glutamic-oxalacetic transaminase showed similar fluctuations.

1455 EFFECT OF ADENOVIRUS TYPE 12 ON TUMOR INDUCTION BY SV40 AND PARA (DEFECTIVE SV40). (E.) Butel, J. S. (Baylor Coll. Med., Houston, Tex.), J. L. Melnick and S. S. Tevethia. *Int J Cancer* 7(1):112-118, 1971.

The tumorigenicity of combined defective SV40 (PARA) and adenovirus was investigated by injecting hamsters with PARA transcapsidated from adenovirus 7 to the Huie strain of adenovirus 12. The PARA-adenovirus 12 inoculum produced SV40-type tumors in 3 of 11 hamsters in approximately 5 wk postinoculation. Twenty wk postinoculation, no tumors had appeared in hamsters given SV40 alone; the latent period for tumors induced by Huie adenovirus 12 was 5 wk. The addition of SV40 to the Huie adenovirus 12 inoculum had little effect on tumorigenicity or latency. In hamsters given Huie adenovirus 12 alone, SV40 and adenovirus 12, or PARA-adenovirus 12, the percentage of animals developing tumors was approximately 50%. PARA-adenovirus 7 and adenovirus 12 produced tumors in 7 of 25 hamsters, beginning 5 wk postinoculation. Tumors induced by PARA-adenovirus 12 contained SV40 and adenovirus tumor antigens, while tumors induced by virus combinations lacking PARA lacked SV40 antigen. SV40 trans-plantation antigen was detected in tumors induced by PARA-adenovirus 12.

1456 ADENOVIRUS TYPE-12-INDUCED TUMOR IN MICE: CHARACTERIZATION OF A TUMOR CELL LINE. (It.) Pauluzzi, S. (Inst. Infect. Dis., U. Perugia, Italy), M. P. Zeppa and A. Piras. *Boll Ist Sieroter Milan* 49(5):448-460, 1970.

Adenovirus type 12 (8.5×10^5 PFU) inoculated into 13 newborn C3H/He inbred mice induced transplantable s.c. tumors in 3 mice after an average latency period of 173 days. Both *in vivo* and *in vitro* (mouse embryo cell cultures) virus-induced neoplastic structures appeared to be undifferentiated and consisted of clusters of small embryonal type cells specific to adenovirus type 12-induced tumors. The continuous cell line obtained from these tumors was transferred *in vitro* through 80 passages and appeared to have medium sized cells with a saturation density of 302,000 cells/cm². The oncogenicity of these cells appeared to be low when inoculated s.c. and much higher when inoculated intracerebrally. Specific tumor antigens were detected as fleck structures within their cytoplasm and as fine granules within the nucleus. Immunity to adenovirus type 12-transformed cells could not be induced.

1457 DEVELOPMENT OF NONONCOGENIC SA7-ADENOVIRUS 2 POPULATIONS THAT IMMUNIZE AGAINST SA7-TRANSFORMED CELLS. (E.) Kaplan, P. M. (Baylor Coll. Med., Houston, Tex.), J. L. Melnick and S. S. Tevethia. *J Nat Cancer Inst* 46(3):565-576, 1971.

Green monkey kidney cell cultures infected with simian adenovirus 7 (SA7) and human adenovirus 2 (Ad2)

yielded populations of SA7-Ad2 virus which, when treated with anti-SA7 or anti-Ad2 antiserum and inoculated into green monkey cell cultures, showed that the SA7-Ad2 virus had the antigenic properties of the Ad2 parent; anti-Ad2 antiserum completely inhibited plaque formation by the virus. All SA7-Ad2 populations induced synthesis of SA7 tumor antigen in simian cells; the SA7 tumor antigen was located in both nucleus and cytoplasm of infected cells. Ad2 antiserum, but not SA7 antiserum, inhibited the induction of synthesis of tumor antigen, suggesting that the genome which coded for SA7 tumor antigen existed within an Ad2 viral coat. Progeny virus from plaques induced in human embryo kidney cells by SA7-Ad2 virus grew in human embryo kidney cells but not in simian cells, while progeny from plaques produced in simian cells by SA7-Ad2 grew in human and simian cells. Plaque formation by SA7-Ad2 virus in simian cells was enhanced more than 10-fold by infection of cells with excess helper Ad2 virus. Plaque formation by SA7-Ad2 in simian cells showed 2-hit kinetics, suggesting that the virus particle which complemented plaque formation by Ad2 in the previous experiment is defective and cannot replicate independently of helper Ad2 virus. Although simian cells were abortively infected by Ad2, cells infected with both SA7 and Ad2 showed a 2,500-fold increase in virus production from 6-72 hr after virus infection. SA7-Ad2 virus containing the defective SA7 complementarity particle produced no tumors in hamsters, but SA7 alone induced tumors in 65% of inoculated hamsters; SA7-Ad2 virus did induce SA7 transplantation immunity in hamsters.

- 1458 A TEMPERATURE-SENSITIVE MUTANT OF ADENOVIRUS 31, DEFECTIVE IN VIRAL DEOXYRIBONUCLEIC ACID REPLICATION. (E.) Suzuki, E. (Nat'l. Inst. Hlth., Tokyo, Japan) and H. Shimojo. *Virology* 43(2):488-494, 1971.

The physiological activity of a temperature-sensitive mutant (ts 13) of adenovirus 31 was analyzed by means of DNA polymerase and thymidine kinase activity monitoring. The ts 13 mutant induced synthesis of T antigen, DNA polymerase and thymidine kinase but did not synthesize viral DNA and capsid protein at the nonpermissive temperature (39.5°C). The temperature shift-down test showed that the function of a gene ts 13 must be expressed for viral DNA replication during the period of 16-24 hr postinoculation, whereas the temperature shift-up test showed that protein synthesized at low temperatures was either rapidly exhausted or inactivated at high temperatures. Although tumors were produced in hamsters by ts 13 at 37.5°, it is not known whether transformation of cells occurs at nonpermissive temperatures.

- 1459 HAMSTER TUMORS INDUCED BY TYPE I AVIAN ADENOVIRUS (CELO): I. HISTOPATHOLOGY AND NEOANTIGEN OF VIRUS-INDUCED AND TRANSPLANTED TUMORS. (E.) Miller, L. T. (Dept. Anim. Path., U. Rhode Island, Kingston), V. Jasty, L. O. Mancini and V. J. Yates. *Arch Ges Virusforsch* 32(2-3):221-228, 1970.

Chicken-embryo-lethal-orphan avian adenovirus type I (CELO) were injected into hamsters in amounts of 0.1

ml of virus suspension; other hamsters were given transplants of CELO-induced fibrosarcomas or injections of tumor homogenates. Twenty-nine fibrosarcomas were induced by these procedures in the dorsolateral region or cheek pouches, and the tumors ranged in size from 7-90 mm in diameter. Tumors induced by viral inoculation and by transplant were similar histologically; all were fibrosarcomas with areas of increased vascularity, hemorrhage and necrosis. Variable amounts of intercellular collagen were found, depending on the extent of differentiation attained by the tumors. Virus-induced tumors showed cellular pleomorphism with prominent bizarre multinucleated giant cells; transplanted tumors showed fewer bizarre giant cells and increased mitotic activity. Results of immunofluorescence tests indicated a CELO-specific antigen in virus-induced and transplanted tumors; in all cases, fluorescence was restricted to the cytoplasm surrounding the nuclear envelope. Viral antigen was not detected.

- 1460 INFLUENCE OF HOST CELL ON BIOLOGIC MARKERS OF TYPES 1 AND 2 *HERPESVIRUS HOMINIS*. (E.) Stubbs, K. G. (Med. Ctr. U. Alabama, Birmingham), E. Snider and C. A. Alford, Jr. *J Infect Dis* 123(1):169-177, 1971.

The infectivity of wild *Herpesvirus hominis*, types I and II, was investigated in primary rabbit kidney cells, diploid human lung cells, primary human amnion cells, and African green monkey kidney (AGMK) cells. At 24 hr after infection of cultures with virus, *Herpesvirus hominis* type I produced amounts of infectious virus comparable to that produced by *Herpesvirus hominis* type II; however, virus titers produced by type I were somewhat higher than titers produced by type II, a difference especially notable in human diploid lung cells and primary human amnion cells. By 48 and 72 hr postinfection, extracellular infectivity of type I was consistently and markedly higher than that of type II in all cell systems except AGMK cells. In primary rabbit kidney cells, diploid human lung cells, and primary human amnion cells, type I extracellular infectivity was higher than that of type II by 6-20 fold at 24 hr, 8-800 fold at 48 hr and 25-600 fold at 72 hr. In AGMK cells, infectivity of type I and type II remained similar through 72 hr postinfection, with type II infectivity slightly higher than type I infectivity as a rule. Cell-associated infectivity of type I virus was also higher than that of type II virus in primary rabbit kidney cells; type II had higher levels of cell-associated infectivity than type I in AGMK cells. Infectivity of type I virus in AGMK was 50 times more sensitive to inhibition by 5-iodo-2-deoxyuridine than type II virus. Both differential infectivity characteristics and susceptibility to inhibition by 5-iodo-2-deoxyuridine were retained by the 2 types of virus through repeated cell passages, indicating that these 2 properties of the virus types may be useful markers for recognizing wild type *Herpesvirus hominis*.

- 1461 ISOLATION AND CHARACTERIZATION OF A HERPESVIRUS-LIKE (HSIUNG-KAPLOW) VIRUS FROM GUINEA PIGS. (E.) Bhatt, P. N. (Yale U. Sch. Med., New Haven,

onn.), D. H. Percy, J. L. Craft and A. M. Jonas.
Infect Dis 123(2):178-189, 1971.

herpeslike virus which demonstrated a spontaneous cytopathic effect (CPE) was recovered from guinea pig lung and kidney cell cultures and from trypsinized kidney cell cultures. The virus was isolated from 13 of 17 lung-explant cultures, from 2 of 12 kidney explant cultures, and from 10 of 15 trypsinized kidney cell cultures. No CPE was produced by inoculating guinea pig kidney cell cultures with supernatant from triturated virus-positive tissue cultures. Spontaneous CPE usually appeared within 1-2 wk in trypsinized kidney cultures, and in 2-3 wk in lung-explant cultures. Virus extracted from infected cultures inoculated into other guinea pig cell cultures resulted in the production of viruses by the inoculated cultures; kidney cell cultures showed the highest titers of virus ($6.7-7.0 \log_{10}/0.1 \text{ ml}$). The herpeslike virus was neutralized by rabbit antisera prepared against a previously isolated herpeslike virus and the latter virus was neutralized by antisera to the newly-isolated herpeslike virus. 5-Bromodeoxyuridine at concentrations of 10^{-5} M inhibited the multiplication of the virus in guinea pig kidney cell cultures. The virus produced no pathological effects in experimentally inoculated guinea pigs, mice, rhesus monkeys or hamsters. This newly-isolated herpeslike virus is apparently not the cytomegalovirus of the guinea pig; but seems to exist as a latent infection in guinea pig strains.

1462 STRUCTURAL PROTEINS OF HERPES SIMPLEX VIRUS. (E.) Robinson, D. J. (Scottish Horticult. Res. Inst., Invergowrie, Dundee) and D. H. Watson. *J Gen Virol* 10(2):163-171, 1971.

A method for purification of herpes virus by means of fluorocarbon treatment, ultracentrifugation, sucrose gradient centrifugation and chromatography, and a description of the pattern of structural polypeptides of these purified preparations is reported. Preliminary stages achieved 50-fold concentration, 10-fold purification and 10-20% recovery of virus particles. Under the conditions of growth, 5-10% of the original yield of virus particles possessed envelopes and the concentrated virus obtained by ultracentrifugation had a protein content of $3.9 \mu\text{g}/10^{10}$ particles. The final preparation was virtually free of diffusible antigens which gave no lines in immunodiffusion tests using antisera either against cells infected with herpes virus or against uninfected cells; the particle/infectivity ratio of purified virus was 3-6 times greater than that for the crude virus. Samples of purified virus with labeled amino acids showed a complex band A containing about 50% of the recovered radioactivity and appeared to consist of at least 2 major components. The patterns obtained in polyacrylamide electrophoresis reflect the polypeptide composition of naked particles, suggesting that the nucleocapsids of herpes simplex virus are composed of at least 8 polypeptides.

1463 DIFFERENTIAL EFFECT OF 7,12-DIMETHYLBENZ-(a)ANTHRACENE ON INFECTIVITY OF HERPES SIMPLEX VIRUS TYPE 2. (E.) Docherty, J. J. (Milton

S. Hershey Med. Ctr., Pennsylvania St. U., Hershey), R. J. Goldberg and F. Rapp. *Proc Soc Exp Biol Med* 136(1):328-333, 1970.

The effect of incubation with 7,12-dimethylbenz(a)-anthracene (DMBA) on the infectivity of herpes simplex virus types 1 and 2 was investigated in cultures of rabbit kidney cells. Cells were infected with virus and incubated with DMBA in amounts of 10, 50 or 100 $\mu\text{g}/\text{ml}$ of culture. Virus titers obtained when the infected cells were incubated alone, with anthracene or with dimethylsulfoxide after 24 hr were comparable (titers of 5.0×10^5 plaque-forming U (PFU)/ml for cells incubated with anthracene and 1.9×10^6 PFU/ml for cells incubated with dimethylsulfoxide). Infected cells grown with DMBA showed markedly lower titers (1.3×10^4 PFU/ml after 24 hr). Incubation with DMBA in amounts of 100 or 50 $\mu\text{g}/\text{ml}$ reduced the infectivity of herpes simplex virus by 99%, while incubation with the other agents reduced infectivity 0-24%. The inactivation of virus by DMBA was found to be maximal when cells were incubated at 37°; herpes simplex virus type 2 was more susceptible to inactivation by DMBA at all temperatures than herpes simplex virus type 1; at 1°, DMBA reduced the infectivity of virus type 1 by 38%, while at the same temperature, DMBA incubation reduced the infectivity of virus type 2 by 61%.

1464 ACUTE LYMPHOCYTIC LEUKEMIA IN OWL MONKEYS INOCULATED WITH HERPESVIRUS SAIMIRI. (E.) Melendez, L. V. (Harvard Med. Sch., Southboro, Mass.), R. D. Hunt, M. D. Daniel, B. J. Blake and F. G. Garcia. *Science* 171(3976):1161-1163, 1971.

Peripheral blood changes characteristic of leukemia induced by herpesvirus saimiri inoculation (i.v., s.c., or intradermal) were studied in the owl monkey. Six animals died between 11 and 14 wk after the initial virus inoculation; 2 exhibited histopathological findings of malignant lymphoma accompanied by invasion of lymph nodes, spleen, liver, kidney and heart with lymphocytic cell types. Three animals exhibited hyperplasia of lymphocytes in lymph nodes with hepatic sinusoids containing excess numbers of lymphocytes; one animal with no signs of malignant lymphoma or lymphocytic hyperplasia died of an undetermined cause. Of 6 animals reinoculated in the 23rd wk, 4 died with gross and histopathological features of lymphocytic malignant lymphoma; 1 animal developed lymphocytic leukemia 1 wk prior to reinoculation; 2 developed leukemia with a total white cell count in excess of $90,000/\text{ml}^3$ 3 wk and 1 wk post-reinoculation, resp. Two animals killed at 36 wk showed no lesions. The incidence of malignant lymphoma in this study was 50% compared with 100% of all owl monkeys inoculated in earlier studies, with the course of the disease extending to 36 wk compared to prior survival times of 4 wk with the use of dilute inoculum. Variation in virus virulence or host variation may influence the pathogenicity of herpesvirus saimiri in the animal.

1465 ULTRASTRUCTURAL STUDIES OF A HERPESVIRUS OF TURKEYS ANTIGENICALLY RELATED TO MAREK'S DISEASE VIRUS. (E.) Nazerian, K. (ARS Reg. Poultry

Res. Lab., East Lansing, Mich.), L. F. Lee, R. L. Witter and B. R. Burmester. *Virology* 43(2):442-452, 1971.

Electron microscopic observation of duck embryo fibroblasts, chicken embryo fibroblasts, and chicken kidney cell cultures transformed by a herpesvirus of turkeys (HVT) showed HVT-transformed cell nuclei to contain large numbers of small (35 nm) hexagonal particles. The nuclear particles in HVT-transformed cells appeared in aggregates and occasionally took the form of crystals; in Marek's disease virus (MDV)-infected cells, particles were found singly when found at all and never appeared as crystals. In MDV-infected cells, particles were present only along with typical herpesvirions while in a few of the HVT-infected cells, the particles were seen in the absence of herpesvirions. HVT-infected cells contained crystalline arrays composed of particles having the size and electron density of ribosomes. Polykaryocytosis was found in both MDV- and HVT-infected cells; with infected duck embryos, the polykaryocytes were larger than those in the other cultures used. Nuclear inclusion bodies were more frequent in HVT- than in MDV-infected cells, but the bodies were similar and consisted of naked virions in both cases. The nucleocapsids of HVT- and MDV-infected cells were morphologically alike, having an electron-dense core; however, the nucleocapsids of the 2 virions differed in some morphological details. Certain nucleocapsids of HVT lacked the electron-dense core and contained several particles attached to the inner side of the capsid arranged in such a way as to give the viral core the form of an electronlucent cross. Envelopment of the nucleocapsid occurred in both HVT- and MDV-infected cells.

1466 INVESTIGATION OF ANTIGENIC RELATIONSHIP OF MAREK'S DISEASE, HERPES VIRUS AND EB VIRUS (HERPES-TYPE VIRUS). (E.) Stevens, D. A. (U. Med. Ctr., Stanford, Cal.), S. D. Kottaridis and R. E. Luginbuhl. *J Comp Path* 81(1):137-140, 1971.

The possibility of cross-reactivity between Epstein-Barr virus (EBV) and the viral agent of Marek's disease in chickens (MDHV) was investigated; immunodiffusion and immunofluorescence tests were run with human anti-EBV serum and infected chicken or rabbit anti-infected chicken MDHV antiserum. Results of homologous immunofluorescence testing of human serum against EBV antigen and anti-MDHV serum against MDHV antigen were invariably positive; however no cross-reactivity between anti-EBV serum and MDHV antigen or between anti-MDHV serum and EBV antigen were observed. Results in immunodiffusion tests with EBV and MDHV infected cell antigens were essentially identical to the results of immunofluorescence tests: reactions were seen only in homologous tests. However, precipitating antibody was found in 1 test in 3 of 4 Marek's disease-infected birds to an antigen in the EBV preparation. Apparently, EBV and MDHV do not enter into antigenic cross-reactions, and do not share antigens.

1467 PATHOGENICITY AND ANTIGENICITY OF CLONES FROM STRAINS OF MAREK'S DISEASE VIRUS AND THE HERPESVIRUS OF TURKEYS. (E.) Purchase, H. G. (Anim. Sci. Res. Div., Agric. Res. Serv., East Lansing, Mich.), B. R. Burmester and C. H. Cunningham. *Infect Immun* 3(2):295-303, 1971.

This paper describes the purification by cloning of three strains of Marek's disease virus and one of the herpesvirus of turkeys, their pathogenicity as observed in chickens, and their antigenicity as characterized by the use of indirect fluorescent-antibody and agar-gel precipitin tests. Of 50 attempts to filter viruses, 36% were successful with the herpesvirus of turkeys and showed a maximum number of 250 plaques as compared to 9 to 20 plaques for Marek's disease virus. Of the Marek's disease virus strains studied, the JM19 clone killed about 80% and the JMHP clone killed 0% of the chickens, and they induced 90 and 0% lesions, resp. Strains GA and RPL39 produced intermediate levels of mortality and a higher incidence of visceral lesions, while the herpesvirus of turkeys was nonpathogenic. All clones, including the herpesvirus of turkeys, contained the B antigen; JM19, JM34, JM35, JM36, RPL39 and GA gave evidence of A and other antigens while clones JM30, JM31, and JMHP lacked the A antigen. In plaques produced by clones with A antigen, a diffuse antigen in the cytoplasm of infected, morphologically normal cells surrounded the plaques stained with homologous antiserum. Herpesvirus of turkeys and Marek's disease virus can be distinguished by differences in intensity and distribution of staining antigen.

1468 EVALUATION OF THE CHICKEN IMMUNE RESPONSE TO MAREK'S DISEASE HERPESVIRUS. (E.) Zacharia, T. P. (Rockefeller U., New York, N. Y.). *J Reticuloendothel Soc* 9(2):138-146, 1971.

The immune response to sheep red blood cells of chickens infected with Marek's disease herpes virus was investigated. Chickens were infected with the virus various ages up to 6 wk; thereafter, sera were extracted and absorbed with 0.1 ml of sheep red blood cells and antigenic reactions were noted. There was a high correlation between the incidence of virus-associated gonadal and dorsal root ganglia tumors and elevated anti-virus antibody titers. In chickens exposed naturally or parenterally to virus the reciprocal mode hemagglutinin titer was 128. The immunocompetence of the herpes virus-infected chickens inoculated at 6 wk-of-age with sheep red blood cells was not depressed, and anti-virus antibody titers had modes of 6 (\log_2 titer) in this group; inoculated virus-infected and control chickens not exposed to virus had reciprocal mode titers of 64 and 128, resp. The anamnestic response to sheep red blood cell antigens was not depressed in virus-infected birds; reciprocal mode titers of 512 and 256 were recorded for the virus-immunized and sheep red blood cell inoculated birds, and for sham-inoculated birds resp.

- 1469 IDENTIFICATION OF THE NUCLEIC ACID OF MOUSE MAMMARY TUMOR VIRUS (MTV) USING FLUORESCENCE MICROSCOPY. (E.) El-Fiky, S. M. (Med. Res. Inst. Alexandria, United Arab Republic), N. H. Sarkar and D. H. Moore. *Acta Histochem* 37(2): 323-329, 1970.

The specificity of the acridine orange staining technique used for identification of RNA of the mouse mammary tumor virus has been tested by fluorescence microscopy. Dried droplet preparations of concentrated virions of Rauscher murine leukemia, influenza, mammary tumor virus and nucleoids of mammary tumor virus fluoresced a flame-red in blue-violet light while smears of reovirus showed a yellow-green fluorescence, indicating a double-stranded RNA; vaccinia virus preparations showed brilliant apple-green fluorescence indicating also the presence of double-stranded DNA. After nuclease digestion (RNase, DNase) as well as digestion with 0.5% pepsin, no change in fluorescence of B particles was observed, but treatment with pepsin, trypsin and deoxyribonuclease resulted in pale orange fluorescence. After treatment with the proteolytic enzymes and ribonuclease, the B particles were readily susceptible to ribonuclease action and showed green fluorescence; following incubation either with pepsin or ribonuclease, the fluorescence was flame-red. Following staining with acridine orange, the nucleoid fraction of P particles gave flame-red fluorescence, while the membrane fraction fluoresced green. These results provide convincing evidence for the single-stranded nature of the mammary tumor virus RNA in confirmation of earlier reports.

- 1470 STUDIES ON THE MOUSE MAMMARY TUMOR AGENT (MTA): II. CYTOCHEMISTRY OF AMINOPEPTIDASE IN NORMAL MAMMARY GLAND OF C57BL, SPONTANEOUS AND VIRUS-INDUCED MAMMARY TUMORS IN R III AND C57BL MOUSE STRAINS, RESPECTIVELY, AND IN CELL LINES PRODUCING THE MAMMARY TUMOR VIRUS. (E.) El-Fiky, S. M. (Inst. Med. Res. Alexandria, Egypt, UAR). *Acta Histochem* 38(1):181-188, 1970.

Intracytoplasmic granules associated with aminopeptidase were found in normal mouse mammary epithelial cells and in cells of virus-induced and spontaneous mammary adenocarcinomas in mice. In normal mammary glands, granules were grouped in localized aggregates, while in tumor tissue, granules were evenly distributed in the cytoplasm. The granular reaction was found to be most intense in tumor cells from strain RIII mice, followed by C57BL virus-induced tumor cells, and C57BL normal mammary cells. A granular aminopeptidase reaction was also found for cells in culture; enzyme activity was at a higher level in cells producing the mammary tumor virus than in normal cells, suggesting that increased aminopeptidase activity was not a cell reaction but was that of the virus particles.

- 1471 MAMMARY TUMORS, PLAQUES, AND HYPERPLASTIC ALVEOLAR NODULES IN VARIOUS COMBINATIONS OF MOUSE INBRED STRAINS AND THE DIFFERENT LINES OF THE MAMMARY TUMOR VIRUS. (E.) Heston, W. E. (Natl.

Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and G. Vlahakis. *Int J Cancer* 7(1):141-148, 1971.

Mammary tumors were developed with frequencies ranging from less than 1 to 100% by each of the following inbred mouse strains: C3H, C3HfB, C3HfDD, C3H-A^{VY}, C3H-A^{VY}fB, DD, DDfB, DDfC3H, BALB/c BALB/cfDD, BALB/cfC3H, A(High), A(Low), AfB and C57BL. The highest incidence of mammary tumors was found in C3H-A^{VY} mice (100%), and the lowest incidence (less than 1%) in A(Low) and C57BL mice; BALB/cfC3H mice also had 100% mammary tumor incidence. Low tumor incidence was found for AfB mice (1%) and DDfB mice (4%). While BALB/c mice had a tumor incidence of only 20%, BALB/cfDD mice had a tumor incidence of 97%. DDfC3H and C3H mice developed mammary tumors at the youngest average age of 6.8 and 7.2 months, resp.; C3HfB and DDfB mice developed tumors at the highest average age, 18.8 and 19.5 months, resp. Mammary tumor virus antigen was found in all but 4 strains, DDfB, BALB/c, A(Low), and C3HfB. Mammary tumor viruses were found in the milk of 20/27 C3H mice and in 23/28 C3H-A^{VY} mice; no virus was found in milk of C57BL or AfB mice. Virus plaques were the result of DD or BALB/c genotypes and DD virus but not of C3H or A genotype or of C3H or A virus. Hyperplastic alveolar nodules were found in all mouse strains developing mammary tumors; the age at which they first appeared depended on the mouse strain and on the line of virus; nodules appeared at the age of 3 months in DD, C3H and C3HfDD mice.

- 1472 IMMUNOLOGICAL AND PATHOLOGICAL MANIFESTATIONS OF MURINE SARCOMA VIRUS (MOLONEY) INFECTIONS. (E.) Schlom, J. (Coll. Phys. Surg., Columbia U., New York, N.Y.), J. B. Moloney and V. Groupe. *Cancer Res* 30(12):2955-2961, 1970.

In a study of the pathological picture of Moloney murine sarcoma virus (MSV) infections in mice, an inverse relationship was found between latency of tumor development and dilution of MSV inoculum. MSV dilutions of 10^0 - 10^{-2} produced tumors in 100% of mice with latencies of 3.5-7.3 days for 50% tumor incidence (Y_{50}); dilutions of 10^{-3} produced tumors in 90% of mice with latency of 12.2 days for Y_{50} . In mice given virus dilutions of 10^0 - 10^{-3} , tumors regressed in 100-78% of cases after 14-21 days. Mice receiving a 10^0 virus dilution with regressed tumors showed relapse, usually resulting in death, in 40% of cases, while the relapse percentage in mice given 10^{-1} to 10^{-3} virus dilutions was 56% and 43%, resp. The tumors developed rapidly in the left inguinal region injection site, and were characterized as rhabdomyosarcomas; hepatic tumors were also observed. Adult mice susceptible to MSV tumor induction displayed levels of antibody to MSV sufficient to neutralize more than a $10^{3.2}$ median effective dose of virus. Antibody titers were not dependent on initial MSV dose, but increased with increasing duration of tumor before regression. Relapse of mice with regressed tumors was marked by pronounced growth in the mesenchymal region surrounding the splenic follicles of cells which contained many mitotic figures and which were refractory to staining. Leukemoid reactions were also seen in livers examined during relapse. Relapse was also marked by the ap-

pearance of metastatic lesions. Mice immunized against MSV by inoculation of live MSV developed tumors in only 15% of cases following a challenge dose of virus potent enough to cause tumors in 100% of nonimmunized mice.

- 1473 A STUDY OF THE SENSITIVITY OF VARIOUS TISSUE CULTURES TO THE MOLONEY (MOUSE SARCOMA) VIRUS. (Rus.) Kukayn, R. A. (A. Kirkhenshteyn Inst. Microbiol. Riga, U.S.S.R.), L. I. Nagayeva, A. V. Zhilevich and S. D. Nitavskaya. *Vop Onkol* 16(12):31-37, 1970.

The interactions between the Moloney sarcoma virus (MSV) and tissue cell cultures from various animal species were explored in terms of cell morphology, mitotic rates and viral reproduction within the cell cultures. The SV-221 strain of MSV was passaged in BALB/c mice which were sacrificed 7-10 days after the appearance of a tumor; the tumor homogenate was used to infect tissue cultures of BALB/c AKR, C3H mouse embryo fibroblasts, Wistar rat embryo fibroblasts and kidney tissue, human embryo kidney tissue, Syrian hamster embryo fibroblasts and kidney tissue, calf embryo kidney, guinea pig and chicken embryo fibroblasts and transplantable L cells. The most striking morphological changes were noticed in the L cell cultures 24 hr following viral infection, where the regularly distributed polymorphic cells were substituted by a network-like pattern of lengthened cells; one day later round cells focused into islets and remained throughout the observation period. Morphological alterations were noticed mainly in cell cultures which appeared to be capable of supporting viral reproduction (rat embryo fibroblasts and human embryo kidney cells), except for the C3H mouse embryo fibroblasts where no viral reproduction occurred. Viral antigen was detected 2-3 days following infection in L cells, in BALB/c mouse embryo, Wistar rat embryo and Syrian hamster embryo fibroblasts, human embryo, hamster embryo and calf embryo kidney tissue cultures. Inoculation of BALB/c mice with infected cell culture material led to the development of rhabdomyosarcoma at the inoculation site within 7-15 days in 50-80% of the animals. Changes in mitotic activity exhibited no specific features due to the MSV infection. However, virus-induced chromosomal alterations focused in the centromeres, and metaphasic and anaphasic chromosomal retardation was ascertained; a decreased amount of diploid cells was noticed in 8 of the 10 cell cultures. MSV seemed to produce no effects on the rat embryo kidney tissue culture which was thus defined as "not sensitive" to MSV.

- 1474 RECOVERY OF MOLONEY MURINE SARCOMA VIRUS ADDED TO BOVINE MILK. (E.) Burger, C. L. (St. U. New York Upstate Med. Ctr., Syracuse), C. C. Chamberlain, M. C. Barstow and B. C. Maher. *J Nat Cancer Inst* 46(1):121-125, 1971.

Recovery of infectious Moloney murine sarcoma virus (MSV) from bovine milk was attempted through continuous flow centrifugation. Essentially all of the infectivity of the MSV added to the milk (1 g equivalent

of MSV to 50 ml skim milk) was recovered, regardless of whether direct pelleting or rebanding technique were employed. Past failure to detect an active virus agent responsible for bovine leukemia may have been due to inactivation before sampling or low titer of virus.

- 1475 THE PRESENCE OF DEFECTIVE VIRUS PARTICLES IN A MOLONEY SARCOMA VIRUS STRAIN PASSAGE (Rus.) Yakovleva, L. S. (Inst. Exper. and Clin. Oncol. Moscow, U.S.S.R.). *Vop Virusol* 15(6):708-711, 1970.

The titer of a Moloney sarcoma virus (MSV) strain, passaged in BALB/c mice at 18 day intervals and isolated from a tumor maintained in CC57Br mouse fibroblast culture, increased 2-4-fold by addition of a Mazurenko leukosis virus (MazLV) strain obtained from the spleen and lymph nodes of CC57Br mice with Mazurenko's leukosis. This increase in infective titer indicated the presence of defective virus particles (70%) within the studied MSV strain; these particles were able to induce sarcoma in mice only in the presence of the MazLV. The presence of defective MSV particles seemed to indicate that the infective titer of the virus may be subject to variations under natural conditions.

- 1476 STUDIES OF MURINE SARCOMA VIRUS: II. DETECTION OF GROUP-SPECIFIC ANTIGENS BY IMMUNOFLUORESCENCE. (E.) Chuat, J. C. (Hosp. St. Louis, Paris, France), F. Lasquellec, A. M. L'Hirondel and M. Boiron. *Int J Cancer* 7(1):101-111, 1971.

Mouse, rat and hamster cell lines infected with Moloney murine sarcoma virus were examined for the group specific antigen (GS) of the murine tumor virus using antisera prepared in rats bearing tumors induced by the Moloney virus. GS antigen was found in the cytoplasm of mouse and rat cells 15 hr after a single infecting dose. Antigen was also found in cell lines infected chronically with murine leukemia or sarcoma viruses, including Rauscher and Gross viruses. Antigenic reactions were found to be exclusively to GS antigens. Viral envelope antigens detectable initially were located at the cell membrane; their appearance and the appearance of GS antigens showed similar time courses. However, envelope antigenicity decreased as tumor cell lines were passaged on living animals. Two hamster cell lines transformed by Moloney virus were negative for GS antigen. Sera taken from hamsters bearing Moloney sarcoma virus-induced tumors failed to elicit a GS reaction in the hamster cells.

- 1477 FREUND ADJUVANT-STIMULATED DEVELOPMENT OF VIRAL RETICULOSARCOMATOSIS IN CC57BR/MV MICE. (Rus.) Ter-Grigorov, V. S. (P. A. Herzen Sci Res. Inst. Oncol. Moscow, U.S.S.R.), V. M. Bergolz and O. Ya. Moskovkina. *Vop Virusol* 15(6):717-721, 1970.

The effect of complete Freund's adjuvant (FA) on the development of Bergolz virus-induced reticulosis (RS) in CC57BR/MV mice was investigated. Inoculation with leukemogenic amounts of cell

free extracts from tumor nodules associated with A (0.1 ml i.p.) decreased 3-fold the latency period for the development of RS in 100% of the experimental animals. When 10^4 tumor cells and FA were inoculated i.p. 22 of 23 mice developed RS within 1 month while inoculation with RS tumor cells without FA induced RS in 17% of the animals 2 months after inoculation. When 5×10^5 RS cells were injected into mice i.p. 8 days after FA inoculation, 21 of 21 mice died of leukemia 2 wk later, and tumor invasion of the liver, spleen, thymus and lymph nodes was seen in 14 mice 21 days after the inoculation of RS cells. FA stimulation of RS development in CC57BR/MV mice appeared to involve an enhancement of RS virus multiplication induced by the administration of the adjuvant.

478 CONDITIONAL LETHAL MUTANTS OF AVIAN SARCOMA VIRUSES: I. PHYSIOLOGY OF *ts* 75 AND *ts* 149. (E.) Friis, R. R. (U. Washington Sch. Med., Seattle), K. Toyoshima and P. K. Vogt. *Virology* 43(2):375-380, 1971.

Physiological activity of 2 temperature-sensitive mutants of avian sarcoma virus were analyzed by means of complement-fixation and uridine labeling of viral RNA. The half-life for the viruses tested at 41° was 60 min, indicating inactivation kinetics indistinguishable from wild type viruses. Cells transformed by the mutants were only 10% as effective in establishing tumors compared to the tumor-producing ability of the wild type-transformed cells. Rates of heat inactivation, envelope antigenicity and host range were identical to the wild type. Reversion frequencies to wild types were 3×10^{-6} for *ts* 75 and 4×10^{-6} for *ts* 149. Uridine labeling indicated that *ts* 75 infected cells synthesized RNA at 41° in substantial amounts 96 hr after infection. Whether DNA synthesis needed for virus production and for transformation can occur at 41° remains to be investigated.

479 INACTIVATION OF AVIAN SARCOMA VIRUSES WITH UV LIGHT: A DIFFERENCE BETWEEN HELPER-DEPENDENT AND HELPER-INDEPENDENT STRAINS. (E.) Friis, R. R. (U. Washington Sch. Med., Seattle). *Virology* 43(2):521-523, 1971.

The difference in UV radiation target size between Bryan high-titer strain of Rous sarcoma virus and helper-independent avian sarcoma viruses was studied. The helper-independent avian sarcoma viruses were more rapidly inactivated than the helper-dependent Bryan strain showing a survival fraction after 4 min of less than 0.001 - 0.01 vs 0.01 - 0.1. The use of identical cell systems (chick or pheasant embryo fibroblasts) and the comparison of helper-dependent and helper-independent viruses of the same subgroup rules out the effects of the differences of host cells and differences in virus structural properties. The inactivation kinetics appear to reflect a real difference in the size of the genetic target between helper-dependent and helper-independent viruses.

1480 STUDIES ON INHIBITION OF VIRAL ONCOGENESIS: II. INHIBITORY EFFECT OF L-ASPARAGINASE, CLAM LIVER EXTRACT AND METHOTREXATE ON ROUS SARCOMA VIRUS FOCUS FORMATION. (E.) Li, C. P. (Div. Biol. Standards, Natl. Inst. Hlth., Bethesda, Md.), W. G. Jahnes and N. M. Tauraso. *Arch Ges Virusforsch* 32 (2/3):236-243, 1970.

When L-asparaginase was added to primary chick embryo cell cultures 2 hr before or after infection with Rous sarcoma virus (Schmidt-Ruppin strain), viral focus-formation was inhibited; concentrations of 0.2 U of L-asparaginase/ml medium added 2 hr after virus infection resulted in 17-37 foci/culture plate, while the same amount added 2 hr before infection resulted in 47 foci/plate compared to 81-128 foci/culture plate for controls. Concentrations of 0.5 U L-asparaginase resulted in 1-6 virus foci when added 2 hr after infection, and 3 foci when added 2 hr before virus. Clam liver extract, added to cultures 2 hr before or after infection with virus, also inhibited focus formation when the dose of clam liver extract exceeded 10 μ g%; high-multiplicity infections of virus also enhanced the inhibitory effect of clam liver extract. Methotrexate 10^{-5} - 10^{-7} M produced nearly complete focus-formation inhibition when added to cultures 1-2 hr before and up to 3 hr after virus.

1481 INVESTIGATIONS ON THE PRESENCE OF VIRAL PARTICLES IN ROUS TRANSFORMED HAMSTER CELL LINES. (Fr.) Gazzolo, L. (I.N.S.E.R.M., Lyon, France) and G. De-The. *Int J Cancer* 7(1):119-130, 1971.

The electron microscopic examination of 9 hamster cell lines transformed *in vivo* and *in vitro* by Rous sarcoma virus (RSV) is described. The production of RSV by the transformed cells appeared to differ fundamentally in chick cells and in mammalian cells. All the transformed chick cultures produced the virus, but the mammalian transformed cells generally did not produce RSV. The electron microscopic examination confirmed the absence of the viral type C particles in the 7 lines transformed *in vitro*. However, this type of particle was found in the RS₂-TH₂ issue of a tumor induced *in vivo* by *in vitro* transformed cells. The RS₂ cells used for the tumor graft did not produce C particles; those particles found in the RS₂-TH₂ line were morphologically similar to mouse leukemogenic virus. The particles associated with the cell mitochondria of the other line transformed *in vivo* (SR/Cl₂) were similar to intracytoplasmic particles of type A. Only this line of all the lines studied was non-virogenic, in spite of the fact that the cells produced the GS (group specific) antigen. Particles of type R were observed in all the lines.

1482 ISOLATION AND CHARACTERIZATION OF PROTEINS FROM ROUS SARCOMA VIRUS. (E.) Hung, P. P. (Abbott Lab., North Chicago, Ill.), H. L. Robinson and W. S. Robinson. *Virology* 43(1):251-266, 1971.

The number and structure of protein components in the Bryan high titer strain of Rous sarcoma virus

(RAV-1) were studied in chick embryo fibroblasts by means of isoelectric focusing in urea. Seven radioactive peaks with isoelectric points between 3.5 and 9.9 were noted which, upon further analysis, revealed a total of 8 ^{14}C -amino acid-labeled proteins with molecular weights between 14,000 and 96,000 daltons. Three glucosamine labeled components and a 4th glucosamine-labeled component devoid of radioactive amino acids were electrophoretically separated. High complement fixation titers and crossing precipitin lines were demonstrated by two components in agar gel diffusion with hamster anti-serum to avian-tumor virus group-specific antigen. One or more of the proteins could be related to RNase and ATPase.

1483 BEHAVIOR OF CHICK EMBRYO CELLS IN TISSUE CULTURE WHEN INFECTED WITH ROUS SARCOMA VIRUS: I. LOSS OF CONTACT INHIBITION. (E.)

Levinson, W. (Dept. Microbiol., U. California, San Francisco), D. Heilbron and J. Jackson. *J Nat Cancer Inst* 46(2):323-335, 1971.

Contact inhibition was studied in chick embryo cells in tissue culture infected with Rous Sarcoma virus. The estimated mean coefficients of contact inhibition ratios (maximum inhibition = 0) for primary and secondary cell culture infected plates were consistently larger for initial cell concentrations of 2×10^5 or above at 36 hr or more of incubation; increasing the number of cells to as high as 8×10^5 per plate did not decrease the interval below 36 hr. On agar-containing medium, no significant difference in contact inhibition ratios occurred at 24 hr after infection, but at 48 hr the difference was significant at $P < 0.005$. When uninfected cell cultures were counted at 24 hr, the ratios increased from 0.09 with 2×10^5 cells to 0.33 with 8×10^5 cells; with increased incubation time, ratios for 2×10^5 cells increased from 0.09 at 24 hr to 0.44 at 72 hr, indicating that the degree of contact inhibition depends not only on cell density but also on the time of incubation, providing the medium remains unchanged. Infected plates tended to show more variability of number of nuclei than uninfected plates but the increased variability was apparently not related to any of the factors pertaining to experimental conditions.

1484 GLIOMAS INDUCED BY ROUS SARCOMA VIRUS IN THE DOG: AN ULTRASTRUCTURAL STUDY. (E.)

Haguenau, F. (Lab. Exp. Med., Coll. France, Paris), G. F. Rabotti, G. Lyon and A. Morailon. *J Nat Cancer Inst* 46(3):539-559, 1971.

Electron microscopy confirmed that gliomas induced in dogs by intracerebral inoculation of Rous sarcoma virus of the Schmidt-Ruppin strain were subependymal astrocytomas in 21 of 22 animals. The astrocytomas were of the type designated as spongioblastomas or pilocytic astrocytomas. The gliomas were often located in the left ventricle, though the viral inoculation had been on the right hemisphere; tumors occasionally invaded the hemispheres, and protruded into the lumen of the lateral ventricles. The main proliferating cell type of these gliomas had a clear

nucleus, a convoluted plasma membrane, filamentous cytoplasm and unusually small mitochondria. Crystal line arrays of filamentous material were seen in the cisternae of the ergastoplasm; these inclusions were not found in astrocytes, but they were often found in endothelial cells, and their significance was unknown. These crystalline aggregates may have been artefacts of viral infection in the cells. However, no virus particles were found in any of the glioma cells.

1485 SIZE DIFFERENCES AMONG THE HIGH MOLECULAR WEIGHT RNA'S OF AVIAN TUMOR VIRUSES. (E.)

Bolognesi, D. P. (Max Planck Inst. Virus Res., Tübingen, Germany) and T. Graf. *Virology* 43(1):214-222, 1971.

Sedimentation behavior of high molecular wt RNAs from avian tumor viruses (Rous sarcoma virus, Rous-associated virus and avian myeloblastosis virus strains) was studied by means of gel electrophoresis and sucrose gradient sedimentation analyses. Sedimentation properties revealed 3 high molecular wt RNAs designated as large (SRV-1), medium (MAV-BO), and small (SRV-H) molecules. In acrylamide-agarose gel separation a linear relationship was obtained with RNAs having a molecular wt below 2×10^6 daltons. A 6% difference in sedimentation in sucrose gradient between large and small molecules was noted, which represents a rather large portion of nucleic acid. Size differences were not directly related to its ability to produce tumors in mammals.

1486 PRESENCE OF VIRAL GENOME IN CHINESE HAMSTER EMBRYONIC CELL TRANSFORMED *IN VITRO* WITH BRYAN STRAIN OF ROUS SARCOMA VIRUS (B-RSV).

(E.) Hlozaneck, I. (Inst. Exp. Biol. Genet., Prague Czechoslovakia). *Progr Immunobiol Stand* 3:53-56, 1969.

Chinese hamster embryo cells cultured with Rous chicken sarcoma virus (Bryan strain) resulted in the transformation of the infected hamster cells within 6-8 wk. Transformed hamster cells did not produce tumors when inoculated into neonatal hamsters, but inoculated chickens developed typical Rous sarcomas which could be passaged as cell suspensions in chickens. Attempts to transfer sarcomas by a cell-free filtrate, however, did not induce tumors in recipients; preparations from the chicken sarcomas did not produce virus either. However, when chicken tumor cultures were superinfected with Rous associated helper virus, the non-productive cultures produced infectious virus.

1487 IDENTIFICATION OF VIRUS-SPECIFIC RNA IN CELLS INFECTED WITH ROUS SARCOMA VIRUS.

(E.) Garapin, A. C. (Dept. Microbiol., U. California San Francisco), J. Leong, L. Fanshier, W. E. Levinson and J. M. Bishop. *Biochem Biophys Res Commun* 42(5) 919-925, 1971.

RNA containing nucleotide sequences identical to those of the Rous sarcoma virus genome were identified in cytoplasmic and nuclear fractions of virus-infected and transformed cells. Equilibrium centri-

fugation on Cs₂SO₄ gradients showed that virus-specific DNA could anneal to RNA extracted from infected cells; virus-specific RNA was found in both cytoplasm and nuclei. No DNA:RNA hybrids were formed if either the DNA was incubated with RNA from uninfected cells or if a mixture of enzymatic product and RNA from uninfected cells was analyzed in Cs₂SO₄ without prior incubation at 37°. The DNA:RNA hybridization appeared to be specific, and the presence of DNA at the density of RNA was not merely fortuitous. The RNA containing nucleotide sequences similar to those of the viral genome comprised approximately 0.5% of the total RNA extracted from virus-infected cells. It was also possible to detect the DNA:RNA hybrids using a step-wise elution from hydroxyapatite.

- 1488 SOME PROBLEMS OF DETECTION OF GENOME OF ROUS SARCOMA VIRUS IN HETEROLOGOUS CELLS. (E.) Simkovic, D. (Cancer Res. Inst., Bratislava, Czechoslovakia) and B. Adamcova. *Progr Immunobiol Stand* 3:49-52, 1969.

Tumorigenicity of 3 rat tumor cell lines transformed by avian tumor viruses was investigated in chicks and rats; the tumor cell lines were rat embryo cells transformed *in vitro* by Rous sarcoma virus (TWERC), rat tumor cells induced *in vivo* by Rous sarcoma virus and maintained in cell culture for 5 yr (XCtc), and rat tumor cells transformed by Bratislava 77 virus (17/RBI/77). All 3 tumor cell lines induced rapidly growing sarcomas in newborn rats even at the low dose of 10³ cells/rat. Living TWERC cells injected into chicks failed to produce tumors; however, XCtc and 17/RBI/77 cells produced tumors in 11/27 and 14/18 chicks, resp. When disintegrated cells or cell free culture fluid was injected, only the 17/RBI/77 cells were tumorigenic. These results suggested that rat tumor cells transformed by avian tumor viruses may contain the viral genome in 3 different states: virus-producing (e.g., 17/RBI/77), virogenic (e.g., XCtc), and non-virogenic (e.g., TWERC). TWERC and XCtc cells contained the same tumor-specific transplantation antigens, but 17/RBI/77 cells did not show tumor specific transplantation antigen.

- 1489 INACTIVATION OF THE TRANSFORMING CAPACITY OF SV40 AND THE ONCOGENICITY OF ADENOVIRUS 12 BY ULTRAVIOLET IRRADIATION. (E.) Yamamoto, H. (Nat'l. Inst. Hlth., Tokyo, Japan). *Jap J Microbiol* 14(6):487-493, 1970.

Results of ultra-violet inactivation of simian virus 40 (SV40) and adenovirus 12 (Ad 12) on the transforming capacity of SV40 and the oncogenic capacity of Ad 12 were studied in baby mouse (C3H/He) brain tissue which was minced and grown in 10% calf serum and in hamsters, resp. The transforming capacity of SV40 was about 4 times more resistant to UV-inactivation than its infectivity; the percentage of survivals in plaque-forming units and focus-forming units relative to unirradiated controls were approximately 2-3% and 50%, resp., after 8 min of irradiation. Changes in the tumor-producing capacity of

Ad 12 by UV irradiation showed that unirradiated virus produced tumors in 2 out of 13 hamsters, whereas treated virus failed to produce any tumors in 8 hamsters. T antigen was positive in all smeared preparations of tumor cells. The enhancement of tumor induction by irradiation was not observed in the incidence of tumors or in the time of appearance of tumors. The capacity of adenovirus 12 to produce tumors was more resistant to ultraviolet-inactivation than its infectivity.

- 1490 VIRAL SUSCEPTIBILITY OF SV40 VIRUS TRANSFORMED HUMAN, BOVINE AND HAMSTER CELL CULTURES. (E.) Sahnazarov, N. (St. Nicolau Inst. Virol., Bucharest, Rumania), M. Nachtigal, N. Cajal, L. H. Graffe and S. Ionescu-Homoriceanu. *Rev Roum Infra-microbiol* 7(4):311-317, 1970.

The susceptibility to viral infection of human embryo fibroblast and lung, golden hamster and bovine cell cultures transformed *in vivo* and *in vitro* by SV40 virus was studied. In human cell cultures herpes simplex virus multiplied in transformed lung tissue by the 25th wk after inoculation and produced titers similar to those obtained in normal embryo cell cultures. Bovine cell cultures, tested 21 wk after inoculation with herpes simplex, showed a limited multiplication and gave a titer of 1.5-2.5 log lower than that obtained in the non-transformed cell culture, whereas hamster cell cultures, in the course of a 16-day observation period, revealed no cytopathic alterations in response to enteroviral infection. These cultures, however, were susceptible to parainfluenza virus type 3 and vaccinia virus. Infection with herpes simplex virus was seen in chemically induced tumors which offered a substrate with a marked susceptibility to infection with herpes simplex virus. The incomplete cytopathic effect obtained in hamster cell lines inoculated with herpes simplex virus might be attributed to a mixture of cells some of which are susceptible and some of which are resistant to the infective agent.

- 1491 NUCLEOLAR CHANGES ACCOMPANYING THE *IN VITRO* TRANSFORMATION OF HAMSTER AND BOVINE CELLS INDUCED BY SV-40 VIRUS. (E.) Mironescu, S. (C. I. Parhon Inst. Endocr., Bucharest, Rumania), N. Sahnazarov and M. Nachtigal. *Rev Roum Infra-microbiol* 7(4):279-294, 1970.

The SV40-induced transformation of adult golden hamster kidney, newborn golden hamster lung and fetal bovine kidney cell cultures was studied microscopically for nucleolar changes. After an initial decrease, the titer of replicating SV40 in primary cultures of hamster embryo cells was seen to increase slightly and then decrease after 96 hr. Morphological changes seen 140 days after inoculation revealed abnormally lobulated nuclei, the incidence of which decreased thereafter. Mitosis gradually increased with time in newborn hamster lung cultures following inoculation with SV40 but decreased progressively in all other tissue studied. Hamster kidney cell cultures exhibited a biphasic curve with respect to mitotic abnormalities, whereas in the new-born ham-

ster lung cultures a progressive decrease in incidence of abnormal anaphases and telophases occurred to below control levels; bovine kidney cell cultures showed no increase in mitotic abnormalities during the first 15 wk after inoculation but thereafter showed an increasing incidence of abnormalities in both phases. Gradual decreases in nucleolar size toward the end of the observation period were observed with the mean number of nucleoli per nucleus showing striking changes in all cultures; "aniso" nucleoli appeared 60 days after viral infection. S.c. injection of tumor cells into unconditioned golden hamsters resulted in no detectable tumor masses up to 210 days after inoculation. The incidence of anisonucleoliosis closely parallels the increasing frequency of marker 1 chromosomes with both parameters attaining maximal values at about the same time.

- 1492 IDENTIFICATION AND PROPERTIES OF COMPLEX FORMS OF SV40 DNA ISOLATED FROM SV40-INFECTED AFRICAN GREEN MONKEY (BSC-1) CELLS. (E.) Rush, M. G. (New York U. Med. Sch., New York, N. Y.), R. Eason and J. Vinograd. *Biochim Biophys Acta* 228(3):585-594, 1971.

Identification of a complex viral DNA in monolayer cultures of African Green monkey kidney cells infected with simian virus 40 (SV40) is reported. The average circular duplex DNA yield from 50 dishes of confluent cells infected at a multiplicity of 2 PFU/cell and worked up 64 hr after infection was 600 µg DNA. Intracellular (SV40) DNA isolated 60 hr after infection contained about 1% each of catenated dimers and circular dimers with similar amounts of circular trimers. The latter were essentially unaffected by viral growth in the presence of 10 µg/ml ethidium bromide, which contrasts with the induction by this agent of large quantities of circular dimers in other organisms. At present neither the function nor the mechanism of formation of the multiple DNA forms is understood.

- 1493 STUDIES ON RESTRICTED GROWTH OF HERPES-VIRUSES IN SV40-TRANSFORMED CELL LINES. (E.) Geder, L. (Med. Sch. U. Debrecen, Hungary), L. Vaczi and E. Jeney. *Acta Virologica* 15(1):35-46, 1971.

Cultures of human and rodent cells, normal and SV40-transformed, were infected with herpes simplex virus obtained from human conjunctival and genital infections; of the SV40-transformed cells, SV40 production was inducible in 2 strains, which contained large amounts of tumor antigen and were highly oncogenic. Herpes simplex virus grew better in normal hamster fibroblasts and in a line of hamster tumor cells than in SV40-transformed hamster cells of high inducibility, oncogenicity and tumor-antigenicity. The latter cell lines, infected with herpes virus, showed a 1.5-2.5 log unit difference in intracellular, and a 0.5-1.72 log unit difference in extracellular virus titer compared to herpes virus grown in normal cells. Herpes virus obtained from conjunctival exudate produced higher virus titers in normal and in SV40-transformed hamster and human cells than the

herpes virus isolated from the genital lesion. In SV40-transformed human embryonic fibroblasts, the intra- or extracellular virus yields were about 10 times less at 6, 13 and 24 hr postinfection with herpes virus than in normal fibroblasts. Normal cells upon infection with herpes virus produced 8-16 times more complement-fixing antigen than did SV40-transformed cells. However, in normal and transformed cells treated with cytosine arabinoside, equal amounts of early herpes virus-specific soluble antigens were produced. The low yield of infectious herpes virus from SV40-transformed cultures was thought to be due to the presence of a small number of virus-producing cells; herpes virus-specific antigens were produced by transformed cells which did not produce infectious herpes virus. Human cytomegalovirus also grew much better in normal than in SV40-transformed human embryonic fibroblasts, the differences amounting to 2-3 log units.

- 1494 SUPERHELIX DENSITY HETEROGENEITY OF INTRACELLULAR SIMIAN VIRUS 40 DEOXYRIBONUCLEIC ACID. (E.) Eason, R. (Dept. Biochem., U. Glasgow, Scotland) and J. Vinograd. *J Virol* 7(1):1-7, 1971.

The closed simian virus 40 (SV40) DNA species formed in the course of infection of African green monkey cells (BSC-1) with SV40 were examined by application of the density separation method. Closed DNA isolated 60-70 hr after infection consisted of intracellular DNA and viral DNA; the former banded at a higher density than the viral DNA whether treated with Pronase or extracted with sodium dodecyl sulfate, indicating a physical difference in the 2 sets of DNA molecules. In 7 experiments the banding distance between the nicked DNA and the intracellular DNA was 9-3% greater than the distance between the nicked DNA and the viral DNA. The band width at half-height of the intracellular DNA appeared to be 20% larger than the corresponding width for viral DNA; tests for superhelix density heterogeneity showed the intracellular closed DNA to be heterogeneous and to be 3/4 as large as the superhelix density of the viral DNA. Density and light fractions obtained from viral DNA isolated from purified SV40 showed superimposition of the bands and a constant normalized ratio of isotopes across the band, indicating homogeneity. Intracellular closed DNA obtained from ethidium bromide-treated cells mixed with closed intracellular DNA from untreated infected cells showed two overlapping non-superimposed bands; corresponding mixtures of the viral DNA species gave completely superimposable bands. The results indicate homogeneity of both the viral and intracellular DNA obtained from ethidium-bromide-treated cells.

- 1495 SV40 REPLICATION IN PRESENCE OF MONKEY KIDNEY ANTIBODIES. (E.) Bottiger, M. (Karolinska Inst., Stockholm, Sweden). *Progr Immunobiol Stand* 3:34-38, 1969.

Incubation of SV40-infected monkey kidney cells with poliovirus vaccine batches and monkey kidney cell antiserum produced a delay in the cytopathic effect associated with SV40 infection. No delay of cytopathic effect was seen when SV40 was grown in med-

containing normal horse, rabbit or calf sera. SV40 antibodies could not be found in rabbit or horse hyperimmune anti-polio sera. The cytopathic effect of anti-monkey kidney cell serum prepared in rabbits by injections of disrupted monkey kidney cells was tested by incubation of the serum with SV40, poliovirus type 1 (Chat strain) and poliovirus type 3; proportions of anti-monkey serum in the medium ranged from 1:16-1:128. At serum dilutions of 1:16, tube titration titers of SV40 were decreased to 1.5 log₁₀ TCID₅₀ at 10 days postinoculation compared to titers of 6.0 log₁₀ TCID₅₀ for SV40 titrated without anti-monkey serum in the medium. Lower concentrations of anti-monkey serum did not affect SV40 titers appreciably. The apparent toxic effect of the monkey kidney antibodies was reversible to some extent; with removal of the anti-monkey serum by change of medium after 2 hr of incubation, cell cultures regained their normal appearance and SV40 titers recovered. Cross reactions between anti-HeLa cell serum and monkey kidney cells was also observed.

1496 PROPERTIES OF ARGINASE FROM SV40-INDUCED HAMSTER FIBROSARCOMAS AND HAMSTER LIVER TISSUES. (E.) North, J. A. (Dept. Microbiol., Brigham Young U., Provo, Utah), G. Schwebach and J. H. Mangum. *J Nat Cancer Inst* 46(3):615-620, 1971.

Arginase activity was found to be 2-4 times higher in SV40-induced fibrosarcomas in hamsters than in normal hamster liver tissue; enzyme activity in fibrosarcomas ranged from 20-33 μ mole urea/mg/min, while enzyme activity in hamster liver amounted to less than 8 μ mole/mg/min. Two fractions containing arginase activity were obtained from both fibrosarcomas and normal liver by chromatography on CM-cellulose columns. One fraction was found to contain 82% of the total enzyme activity, the other 18%. The two fractions of each tissue exhibited similar Michaelis constants for arginine, as well as similar inhibitor constants for ornithine and canavanine although the Michaelis constant for arginine with arginase from hamster liver was about 3 times higher than that for the enzyme from fibrosarcoma tissue. The canavanine inhibition constant for fibrosarcoma tissue was larger than that for hamster liver tissue, while the ornithine inhibition constant was smaller in fibrosarcoma tissue than in hamster liver. The molecular wt of fractions I and II of arginase from hamster liver were found to be 140,000 and 95,000, resp. The molecular wt for fractions I and II of arginase from fibrosarcoma were, resp., 135,000 and 100,000.

1497 STRUCTURE OF SIMIAN VIRUS 40: V. LOCALIZATION OF THE C-TYPE POLYPEPTIDE CHAINS. (E.) Koch, M. A. (Max Planck Inst. Virus Res., Tübingen, Germany), H. Becht and F. A. Anderer. *Virology* 43(1):235-242, 1971.

The structure of simian virus 40 (SV40) and localization of the C-type polypeptide chains were studied utilizing hyperimmune sera from rabbits and convalescent sera from monkeys experimentally infected with the virus. Infectivity tests showed that the

complex of C polypeptides and the viral DNA did not infect cells with the same efficiency as an equivalent amount of complete virus. Serum from a rabbit immunized with C polypeptide gave a positive reaction with SV40 virions, and empty shells possessed the same reactivity as intact SV40. C polypeptides pretreated with a protease-free DNase had no neutralizing activity and reacted weakly or not at all with SV40 and C polypeptide in the complement fixation and indirect hemagglutination tests. Either greatly reduced immunogenicity or altered antigenic specificity of DNase-treated C polypeptides may explain these findings.

1498 THE *IN VITRO* EVOLUTION OF A GOLDEN HAMSTER LUNG CULTURE INFECTED WITH SV40 VIRUS. (E.) Sahnazarov, N. (St. S. Nicolau Inst. Virol., Bucharest, Rumania), M. Nachtigal, L. H. Graffe, S. Ionescu-Homoriceanu and N. Cajal. *Rev Roum Inframicrobiol* 7(4):319-325, 1970.

Alterations in newborn golden hamster lung cell cultures inoculated with simian virus 40 have been observed through co-cultivation with *Cercopithecus aethiops* kidney cells and direct and indirect staining methods. Subcultivation of the lung cell line at 7-10 day intervals resulted in a slow-forming monolayer of cell islets, nonconfluent and with frequent detritus and developing giant nuclei with increasing numbers of nucleoli in some cells after 55-58 days. Cultures stained with hematoxylin-eosin at different intervals showed a gradual increase in the epithelial component with epithelial predominance occurring after 337 days. The infective virus was present at 7 days after inoculation but was absent by day 26, and the tumoral antigen was not found in the nuclei at 362 days after inoculation; oncogenicity was not observed at 308 days after inoculation. Cytogenetic analysis of the lung cell culture at passage 2 showed that 26% of the cells had a diploid number of chromosomes, and 26% had a tendency toward hypotetraploidy. At passages 6 and 50, variation of the chromosome number tended toward tetradiploidy with later passages showing numerical increase in chromosomes. In its evolution towards a stable line, hamster lung cultures exhibit a particularly long stationary phase of 8-22 weeks.

1499 INDUCTION OF CELLULAR DNA SYNTHESIS BY SUPERCOILED SV40 DNA IN X-IRRADIATED MOUSE 3T3 CELLS. (E.) Rozenblatt, S. (Weizmann Inst. Sci., Rehovot, Israel) and E. Winocour. *Virology* 43(1):300-303, 1971.

DNA synthesis was induced in irradiated mouse cells by inoculating them with supercoiled DNA of SV40 (i. e., DNA component I). Mouse cells were given 5000 rads of X-irradiation to reduce background DNA synthesis prior to infection of the cells with viral DNA. Cell cultures were inoculated with 2×10^5 plaque-forming U of viral DNA. At 29-30 hr postinfection, the proportion of DNA-synthesizing cells in the cultures inoculated with SV40 DNA component I was 10-fold higher than that in the control cultures not inoculated with viral DNA. During the same time inter-

val, the incorporation of ^{14}C -labeled thymidine in the cultures inoculated with viral DNA was about 6-fold higher than in the control cultures. DNA-DNA hybridization experiments showed that the induced DNA synthesis was cellular rather than viral.

- 1500 DENSITY INHIBITION OF MOTILITY IN 3T3 FIBROBLASTS AND THEIR SV40 TRANSFORMANTS. (E.) Gail, M. H. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and C. W. Boone. *Exp Cell Res* 64(1):156-162, 1971.

Density inhibition of motility in cultures of mouse fibroblasts and SV40-transformed mouse fibroblasts was determined on observing position changes over time of selected cells. The motility constant was plotted for 3T3 mouse fibroblasts and virus-transformed mouse fibroblasts; the motility of normal fibroblasts changed little if at all over 24 hr. However, virus-transformed fibroblasts showed motility decreased by a factor of 8 over 24 hr. G, a measure of density inhibition of motility, was computed as $3.22 \mu\text{m}^2/\text{h-cell}$ for normal and $0.19 \mu\text{m}^2/\text{h-cell}$ for transformed cells. After change of culture nutrient medium, the motility of transformed cells was not changed appreciably, but the motility of normal cells decreased by a factor of 3 over 99 hr. This finding eliminated the depletion of a nutritional "locomotion factor" as an explanation for the observed decrease of normal fibroblast motility. Apparently, a strong density inhibition of motility in normal cells reflects a strong mutual adhesivity of these cells.

- 1501 CELLS, INTRACELLS AND SCHIZOGENY: I. SOME NEW LINES ESTABLISHED *IN VITRO* HAVING INTEREST IN CYTOBIOLOGY, CANCEROLOGY AND VIROLOGY. (E.) Valladares, Y. (Natl. Inst. Oncol., City U. Madrid, Spain) and Y. Alvarez. *Rev Esp Oncol* 16(1):23-45, 1969.

New cell lines of human, hamster and mouse origin have been developed through serial passage of "cancer-virus" (CV) and simian virus 40 (SV40) in cultures of embryo tissue from Syrian golden and albino hamsters and strains of SWR mice. A cell line from a CV-induced hamster sarcoma was established which was referred to as TC-CV/INO and produced sarcomas within 2 months after s.c. inoculation in all of 25 inoculated mice. An established line, designated as TC-SV40/INO, was produced from passing SV40 strain PA-57 in MkK cell-line from patas monkey; upon inoculation of LLC-MK₂ derived cell cultures with TC-SV40/INO, cytopathic effects which later disappeared were seen and the culture was maintained only by adding uninoculated LLC-MK₂ derived cells. Hamsters inoculated with TC-SV40/INO cells developed tumors that were evident after 37 days, and death occurred 5 wk after appearance of tumors and 10 wk after inoculation. Hamsters inoculated with TC-CV/INO cells developed tumors within 35-50 days which were smaller in size than those in mice; death occurred after several months. Cancervirus-inoculated mouse embryo cultures, known as ER-CV/INO, promoted tumors within 16 days after inoculation into mice, and

death occurred 19-41 days after the appearance of tumors which caused great skin distention and ulceration. Multi-nucleolated cells, large nucleolus, increased numbers of degenerated giant cells were constant features of all cell lines.

- 1502 THE UPTAKE OF SV40 DNA BY NONPERMISSIVE CELLS IN THE PRESENCE OF DEAE-DEXTRAN. (E.) Howard, B. V. (George Washington U. Sch. Med. Washington, D. C.), M. K. Estes and J. S. Pagano. *Biochim Biophys Acta* 228(1):105-116, 1971.

The uptake of tritiated DNA of SV40 by nonpermissive mouse cells in the presence of DEAE dextran (100 $\mu\text{g}/\text{ml}$) was 7-29% in 20 min after 3 washings. When DEAE dextran concentrations were varied and DNA and DEAE dextran were premixed, the initial attachment of ^3H -DNA to cells and the radioactivity associated with cells after 24 hr were maximal at DEAE-dextran concentrations of 100 $\mu\text{g}/\text{ml}$. When the cells were pre-treated with DEAE-dextran, the optimum uptake of ^3H -DNA was achieved with 3000 $\mu\text{g}/\text{ml}$ of DEAE-dextran. Incubation of cells and DEAE-dextran with concentrations of ^3H -DNA ranging from 10-50 $\mu\text{g}/\text{ml}$ did not affect the uptake of DNA. Both the initial attachment of ^3H -DNA and the amount of DNA associated with cells were maximal after 1 min of incubation; temperature of 5-42° did not affect initial ^3H -DNA uptake by cells; however, maximal 24 hr association of DNA with cells required temperatures of at least 25°. DNA became insensitive to deoxyribonuclease after 30 min of cell contact in the presence of DEAE-dextran. Most of the DNA taken up by the cells was eventually hydrolyzed and excreted from the cells, but a small fraction of the viral DNA (0.5%) was retained in the cell nuclei. The addition of 500 $\mu\text{g}/\text{ml}$ of calf thymus DNA to the cell-DEAE-dextran-DNA mixture did not affect uptake of tritiated DNA. When the infectivity of SV40 DNA was tested in African green monkey kidney cells, it was found that the infectivity of the viral DNA was maximal at DEAE-dextran concentrations of 1000 μg for cultures in which DNA and DEAE-dextran were premixed. Increasing concentrations of added calf thymus DNA decreased the infectivity of the viral DNA in the monkey cells. DEAE-dextran appears to facilitate both the function of the viral DNA with the host cell, and the entry of the viral DNA into the cell.

- 1503 ANALYSIS OF THE MOLECULAR FORMS OF SV40 VIRUS 40 DEOXYRIBONUCLEIC ACID SYNTHESIS IN CYCLOHEXIMIDE-TREATED CELL CULTURES. (E.) Kikuchi (Baylor Coll. Med., Houston, Tex.) and K. Nakajima. *J Virol* 7(1):87-94, 1971.

African green monkey kidney cell cultures were infected with SV40, and the SV40 DNA was labeled with thymidine; infected cultures were then treated with 25 $\mu\text{g}/\text{ml}$ cycloheximide to inhibit DNA synthesis. Viral DNA was extracted and analyzed by cesium chloride ethidium bromide equilibrium centrifugation to determine the forms of DNA produced by cycloheximide-treated virus. By 24-28 hr postinfection, it was found that about half of the labeled DNA produced by the virus was of light buoyant density (nicked circular or

ear DNA forms) and half was of heavy density (superhelical form DNA). By 36-40 hr postinfection, about 80% of the DNA was of heavy density, and about 14% was of light density. Heavy density DNA was found by analysis in velocity sedimentation in neutral sucrose gradients to consist of 70-93% superhelical DNA which sedimented at about 21S; light DNA was found to consist of 3 principal regions made up of nicked circular DNA which sedimented at varying rates of velocity. Cycloheximide treatment did not produce an increase in heavy density, superhelical or closed-circular form DNA. In pulse-chase experiments conducted with or without cycloheximide, radioactive label first appeared in nicked molecular forms of DNA which sedimented faster than open-circular viral DNA; eventually, radioactivity was chased into superhelical form DNA. Polynucleotide ligase concentrations appear to be adequate in cycloheximide-treated SV40-infected cultures and there is no increase in duplication errors causing formation of circular oligomeric forms of SV40 DNA.

1504 DEOXYRIBONUCLEIC ACID REPLICATION IN SIMIAN VIRUS 40-INFECTED CELLS: IV. TWO DIFFERENT REQUIREMENTS FOR PROTEIN SYNTHESIS DURING SIMIAN VIRUS 40 DEOXYRIBONUCLEIC ACID REPLICATION. (E.) Kang, H. S. (Dept. Biochem., Princeton U., N. J.), T. B. Eshbach, D. A. White and A. J. Levine. *J Virol* 7(1):112-120, 1971.

When 10 µg of cycloheximide was added to monolayer cultures of African green monkey kidney cells which had been infected with SV40 large-plaque mutant virus, the synthesis of SV40-specific DNA was inhibited by 99% after 2 hr. Cycloheximide inhibited synthesis of both 25S (replicating) DNA and 21S (mature) DNA equally until 1 hr after treatment; thereafter, the ratio of 25S to 21S DNA increased from 0.3 to 1.0. The amount of 25S DNA synthesized in 1 hr increased from 25% in untreated virus-infected cells to 50% 3-4 hr after the addition of cycloheximide. Removal of cycloheximide from treated infected cultures allowed the return of viral DNA synthesis to normal levels within 3 hr; during recovery the ratio of 25S DNA to 21S DNA remained elevated. Protein synthesis appeared to be required for the conversion of 25S DNA to 21S DNA, as indicated by the accumulation of the former DNA during cycloheximide inhibition of DNA synthesis. The protein-requirement hypothesis was further confirmed by the finding that virus-infected protein-rich growing monkey kidney cells converted 25S DNA to 21S DNA with less delay than protein-poor resting cells; at 20 hr after the addition of an isotope label to cultures, infected growing cultures had produced 50% more DNA than resting cultures. Viral DNA replication was not affected by the incubation of cells with a temperature-sensitive SV40 coat protein mutation.

1505 SV40-TRANSFORMED PROSTATIC CARCINOMA IN THE HAMSTER: EFFECT OF HORMONAL MANIPULATION ON THE GROWTH RATE. (E.) Abdalla, A. M. (Roy. Victoria Hosp., Montreal, Quebec, Canada) and J. A. Oliver. *Cancer* 27(2):468-470, 1971.

The effect of hormonal stimulation on the growth of a virus-induced prostatic carcinoma was investigated

in the hamster. Hamsters of both sexes were given dorsal injections of 5-10 mg of SV40-transformed prostatic tumor tissue obtained from a male hamster. Hamsters were then given injections of estrogen (5 mg), androgen (20 mg), or a progestational agent (10 mg Depo-Provera. Maximum tumor growth was observed in untreated males, with tumors attaining a size of 55 cm³ in 28 wk. Female controls and hamsters given androgens showed similar patterns of tumor growth, while animals treated with estrogen showed depressed tumor growth (38 cm³ tumor volume in 28 wk). Tumor growth in hamsters given the progestational agent was drastically reduced; by 29 wk the tumor volume in this group was 4 cm³.

1506 BEHAVIOUR OF ENZYME SYSTEMS IN CERCOPI-
THECUS AND RHESUS KIDNEY CELLS IN CONSEQUENCE OF SV40 VIRUS ACTION. (E.) De Barbieri, A. (S. Belfanti Inst. Sieroter., Milan, Italy), G. C. Tassi, G. Giacometti and M. E. Scevola. *Progr Immunobiol Stand* 3:136-138, 1969.

The behavior of enzyme systems in monolayers of Cercopithecus and rhesus monkey kidney cells infected with SV40 was investigated. Cultures were inoculated with virus at multiplicities of 2 TCID₅₀/cell. A cytopathic effect was observable only 72 hr after inoculation in the rhesus monolayers; however, a cytopathic effect was observed in Cercopithecus cells 48 hr after virus inoculation. Oxidative enzyme systems were impaired by viral infection in both cell types, while glycolysis, the pentose phosphate cycle, hexokinase, glucose-6-phosphatase dehydrogenase and 6-phospho-D-gluconate oxidoreductase were increased. Transketolase and transaldolase showed oxidative shifts toward the production of ribose-5-phosphate. In Cercopithecus cells, proteolysis was markedly inhibited, while in rhesus cells it increased by 40% over uninfected cells. Glutamic dehydrogenase and amino acid oxidase increased sharply in Cercopithecus cells, but no such increase was seen in rhesus cells.

1507 HUMAN-MOUSE HYBRID CELL LINES AND SUSCEPTIBILITY TO SPECIES-SPECIFIC VIRUSES. (E.) Pollack, R. (Sch. Med., New York U., New York, N. Y.), J. Salas, R. Wang, T. Kusano and H. Green. *J Cell Physiol* 77(1):117-120, 1971.

The susceptibility to infection by species-specific viruses of a human-mouse hybrid cell line was investigated. Viruses tested were poliovirus, SV40, and adenovirus, for which human cells are permissive of infection and mouse cells are not, and polyoma virus, for which mouse cells are permissive and human cells are not. Human-mouse hybrid cells supported poliovirus infection and gave viral yields comparable to those of the respective human parental lines; hybrid cells containing lower numbers of human chromosomes failed to support poliovirus infection. The hybrid cells permitted infection by SV40 and synthesized tumor antigen with a frequency higher than that of the mouse parental line which also permitted infection by this virus. Hybrid cells supported infection by polyoma virus, producing viral yields comparable to those produced by mouse parent cell lines;

human parent lines were not susceptible to polyoma virus infection. While adenovirus did infect human parental cells, it failed to infect mouse parental cells or the hybrid cells.

- 1508 SV40 VIRUS TRANSFORMED PROSTATIC CARCINOMA IN THE HAMSTER: I. COMPARISONS OF LACTATE DEHYDROGENASE ISOENZYMES WITH HUMAN PROSTATIC CANCER. (E.) Abdalla, A. M. (Roy. Victoria Hosp., Montreal, Quebec, Canada) and J. A. Oliver. *Invest Urol* 8(4): 442-447, 1971.

The inhibitory effects of stilbestrol, medroxyprogesterone, hydrocortisone and testosterone on lactate dehydrogenase (LDH) isoenzymes in human prostatic carcinoma and in an SV40 transformed prostatic carcinoma in the hamster were investigated *in vitro*. LDH consisted of 5 isoenzymes numbered according to their electrophoretic mobility as LDH I-V. None of the drugs tested had any effect on the LDH isoenzymes of the hamster or human prostatic tumor except stilbestrol, which inhibited human LDH IV and V almost completely after incubation with 0.375 mg for 3 hr; LDH III was partially inhibited. The LDH isoenzymes of the SV40 virus-transformed hamster tumor appear to differ from those of the human counterpart, as far as the response to stilbestrol inhibition is concerned.

- 1509 STUDIES WITH SV40 - ADENO 7 HYBRID VIRUS. (E.) Vonka, V. (Res. Inst. Immunol., Prague, Czechoslovakia), L. Kutinova and H. Zavadova. *Progr Immunobiol Stand* 3:39-43, 1969.

The growth of the SV40-adenovirus 7 hybrid which exists in 2 forms, the true adenovirus 7 and the defective viral particles consisting of the incomplete SV40 genome enveloped in the adenovirus 7 capsid was studied in the human diploid cell strains LEP-12 and LEP-14 and in green monkey kidney cells (GMKC). Both forms grew well in these strains; in LEP cells, new adenoviruses were detected from 23-38 hr after inoculation of the hybrid virus; in monkey cells, the latent period was shorter, the rise in the titers of both components of the hybrid was more abrupt, and the final titers were higher than in the LEP cells. Infection of dog kidney cells or hamster embryo fibroblasts with the hybrid virus resulted in cell transformation; the transformed cells were virus-free. Hamster cells transformed by the virus were oncogenic for adult hamsters, and some of the tumor-bearing hamsters contained antibodies reacting with both the SV40 and the adenovirus 7 T antigens.

- 1510 SOME PROPERTIES OF POLYOMA VIRUS "T" AND "TUMOUR" ANTIGENS. (E.) Zembala, M. (Med. Acad. Cracow, Poland), W. Ptak and Z. Porwit-Bohr. *Z Immunitätsforsch* 141(1):27-36, 1970.

T antigens obtained from polyoma virus-infected mouse and hamster cells were examined and compared with polyoma virus-induced tumor complement-fixing antigens (PV-TCFA). Mouse embryo, mouse kidney, and

hamster kidney cells were inoculated with polyoma virus at doses of 100 TCID₅₀/cell, and antigens were prepared from infected cultures. Detectable amount of T antigen were found in infected cultures 8-12 hr after inoculation with virus (CF titers of about 2-4 log₂¹ for all cell systems studied). Maximum antigen titers were recorded 24-48 hr postinoculation and titers ranged from 16-32 log₂¹ for the various systems. After 48 hr postinoculation, there was a sharp decrease in T antigen synthesis; however, at day 16 postinoculation, hamster kidney cells resumed T antigen production. No differences in physicochemical properties and serological activity were observed between T antigen and TCFA antigen synthesized in tumor cells. The molecular wt of the proteins active in tests was over 3 x 10⁵ daltons and 1.1-1.5 x 10⁵ daltons. The antigen form with higher molecular weight was thought to be an RNA-protein complex.

- 1511 EFFECT OF PHLEOMYCIN ON POLYOMA VIRUS SYNTHESIS IN MOUSE EMBRYO CELLS. (E.) Iwata, A. (Div. Biol., Kansas St. U., Manhattan) and R. A. Consigli. *J Virol* 7(1):29-40, 1971.

When 25 µg of phleomycin was added to mouse embryo cells infected with polyoma virus at multiplicities of 6.2 x 10⁶-1.0 x 10⁸, synthesis of virus was inhibited in the infected cells. Phleomycin added 4 hr after virus infection produced 96% inhibition of virus synthesis; phleomycin added 30 hr postinfection resulted in a 61% inhibition. The treatment of cells with phleomycin did not affect RNA or protein synthesis by cells; however phleomycin inhibited DNA synthesis, especially in uninfected cells. Uninfected cells treated with phleomycin synthesize about one third as much DNA as infected cells treated with phleomycin. A polyoma virus DNA component and virus antigen occurred in the presence of phleomycin; complete and incomplete virus particles were also found in cultures treated with phleomycin. Synthesis of complete virus was more sensitive to phleomycin treatment than was the synthesis of virus particles. The DNA synthesized in infected phleomycin-treated cells was found to be salt-extractable, as was the DNA in untreated infected cells.

- 1512 EPITHELIAL ORIGIN OF POLYOMA SALIVARY GLAND TUMORS IN MICE: EVIDENCE BASED ON CHROMOSOME-MARKED CELLS. (E.) Dawe, C. J. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), J. Whang Peng, W. D. Morgan, E. C. Hearon and T. Knutsen. *Science* 171(3969):394-397, 1971.

Identification of the tissue type of origin of polyoma virus-induced neoplasms of the submandibular gland of polyoma-free mice of strains C₃H/Bi and CBA/H- was studied using a T₆ chromosome-marker system with a trypsin technique for separating epithelium from mesenchyme of gland rudiment. In 8 consecutive primary tumors arising in reassembled, transplanted 4 arose in reassemblies of CBA/H-T₆T₆ epithelium C₃H/Bi mesenchyme and 4 in the reciprocal combination. Cytogenetic identification of 8 primary and 13 transplanted derivatives showed 110 out of 523 metaphase figures to be host cells on the basis of diploidy

a single T₆ chromosome. The remaining 413 were classified as tumor cells because the karyotype was that of one or the other of the donor of two tissue types re-assembled in transplants and the aneuploid condition of many cells. Fourteen of 186 primary tumor cell metaphases demonstrated aneuploidy whereas 89 out of 198 first and second generation metaphases were aneuploid. In the 1st transplant generation of a tumor arising from a reassembly of T₆T₆ epithelium with unmarked mesenchyme, 42 of 49 tumor cells were hyperdiploid containing 4 T₆ markers, and the remaining 7 contained 2 T₆ markers; in controls 4 of 30 tumor cells contained 4 T₆ markers and 26 cells had only 2 T₆ markers. Histologically all neoplasms at the sites of transplant of intact and reassembled glands were undistinguishable from tumors induced by polyoma virus in indigenous salivary glands. Although mesenchyme plays an essential role during neoplastic transformation, it does not contribute cells to neoplastic populations.

1513 INDUCTION OF MITOCHONDRIAL DNA SYNTHESIS BY POLYOMA VIRUS. (E.) Vesco, C. (Lab. Cell Biol., CNR, Rome, Italy) and C. Basilico. *Nature* 229(5283):336-338, 1971.

The effect of polyoma virus infection on extrachromosomal DNA synthesis was studied in 3R3 mouse cells using ³H-thymidine labeling. Mitochondrial DNA synthesis was increased to 4-6-fold in confluent infected cultures compared to uninfected cultures, while nuclear DNA synthesis increased 25-29-fold. Fractionation by CsCl-ethidium bromide centrifugation showed that most of the mitochondrial radioactivity was incorporated into twisted circular molecules of mitochondrial DNA. The increased rates of synthesis in virus-infected cells in both compartments were smaller than the rates observed in uninfected cultures in the exponential growth phase. The nuclear activity in uninfected cells was less than 2% of that in multiplying cells whereas mitochondrial activity proceeded at 20% the rate of exponentially growing cells, and this difference may be related to the different sensitivity of the 2 synthetic systems to virus infection.

1514 CONTROL OF GLYCOLIPID SYNTHESIS IN A CULTURED HAMSTER CELL LINE. (E.) Robbins, P. W. (Massachusetts Inst. Technol., Cambridge) and I. Macpherson. *Nature* 229(5286):569-570, 1971.

The effect of cell density and polyoma viral transformation on synthesis of glycolipids were studied in a cultured hamster cell line utilizing chromatography and autoradiography. Normal cells growing at the lower cell density ($5 \times 10^3 \text{ cm}^{-2}$) showed much less incorporation of labeled palmitate into ceramide trihexoside, galactosylgalactosylglucosyl ceramide, the aminoglycolipid, β -N-acetylgalactosylgalactosylgalactosylglucosyl ceramide and an unidentified ceramide than cells at a higher density ($5 \times 10^4 \text{ cm}^{-2}$), while virus-transformed cells showed normal synthesis of phospholipids, hematoside and ceramide dihexoside. These results suggest that the lack of complex glycolipids in transformed cells could simply be a reflection of the lack of normal contact inhibition and lack of growth restraint.

1515 ACTIVATION OF POLYOMA VIRUS GENOME IN POLYOMA TUMOR CELLS. (E.) Saito, M. (Sch. Hyg. Serv., Kitasato U., Tokyo, Japan), F. Taguchi, K. Hasegawa, Y. Yoshida and D. Nagaki. *Jap J Microbiol* 14(6):512-515, 1970.

Reinvestigation of the rescue of polyoma virus (PV) from 2 polyoma tumor cell lines, KIT-5/2 and KIT-20/W, using a cell fusion technique is reported. Embryo cells produced completely negative results for polyoma viral antigen synthesis and HA production. PV specific fluorescence was about 3-5% and 10-20% in the 2 respective cell lines compared to control cultures in which neither PV viral antigen synthesis nor HA production could be detected throughout the experiments. Antigen was synthesized in infected kidney cell nuclei and reacted only with anti-PV virion antiserum; it did not react with anti-HVJ, anti-SV40 antiserum or normal rabbit serum. Differences in the PV activation pattern in the two cell lines may be either in the proportion of reactive tumor cells, the number of viral genome per cell or the status of the viral genome in the tumor cell.

1516 TRITIATED THYMIDINE INCORPORATION IN WARTS, KERATIC PAPILLOMAS AND EPIDERMODYSPLASIA VERRUFORMIS. (Fr.) Delescluse, C. (A. de Rothschild Ophthalmol. Found., Paris, France), M. Prunieras, M. Regnier, J. Arouete and C. Grupper. *Arch Derm Syph* 97(5-6):525-533, 1970.

1517 FORMATION OF SV40 IN HETEROKARYONS RESULTING FROM HYBRIDIZATION OF SENSITIVE AND TRANSFORMED CELLS EXPOSED TO UV IRRADIATION. (It.) Monti-Bragadin, C. (Inst. Microbiol., U. Padua, Italy), L. Conventi and G. A. Meloni. *Boll Soc Ital Biol Sper* 46(12):565-569, 1970.

1518 JUVENILE XANTHOGRANULOMA ASSOCIATED WITH CYTOMEGALOVIRUS INFECTION. (E.) Balfour, H. H., Jr. (Minneapolis, Minn.), C. E. Speicher, and D. G. McReynolds and M. E. Nesbit. *Amer J Med* 50(3):380-384, 1971.

See also:

- * (Rev): 1267, 1268, 1273, 1274
- * (Chem): 1326, 1356
- * (Immun): 1519, 1520, 1521, 1522, 1523, 1524, 1525, 1526, 1527, 1529, 1530, 1531, 1532, 1533, 1534, 1535, 1536, 1537, 1538, 1543, 1578

- 1519 INTERFERON INDUCTION IN HAMSTER EMBRYO CELLS AND NEWBORN HAMSTERS INFECTED WITH POLYOMA VIRUS. (E.) Gotlieb-Stematsky, T. (Virus Lab., U. Tel-Aviv, Israel) and A. Vansover. *Arch Ges Virusforsch* 32(2-3):201-208, 1970.

Hamster embryo fibroblast cultures and 1 day old hamsters were infected at varying multiplicities with either of 2 strains of polyoma virus, strain C⁻H⁺ (a highly oncogenic strain) and strain C⁺H⁰ (a mildly oncogenic strain). Interferon was found to be produced in greater amounts by the C⁻H⁺ virus in fibroblast cultures than by the C⁺H⁰ virus; by 10 days postinfection the titer of interferon produced by C⁻H⁺ was 32, while that produced by C⁺H⁰ was 4. Interferon activity in culture was found to be sensitive to heating at 60°, and was lost by digesting cultures with trypsin. Treatment with antipolyoma virus serum did not impair interferon activity; interferon from hamster cells did not affect mouse embryo cells. C⁻H⁺ virus also produced higher titers of interferon in hamsters *in vivo* than did C⁺H⁰ virus; at 28 days after inoculation with C⁻H⁺, hamster internal organ extracts at dilutions of 1:32 showed 32% interference inhibition of challenge vesicular stomatitis virus, while extracts from hamsters given C⁺H⁰ showed zero interference inhibition. The peaks of interferon production were attained at the times when viral multiplication diminished in the hamster organs and when tumors began to appear. While C⁺H⁰ infection did not produce infectious virus, the C⁻H⁺ infection produced 10^{4.5} TCD₅₀ of virus/ml of organ suspension within 7 days after inoculation. HI antibody titers to the C⁻H⁺ variant were high by the second wk after infection; HI antibodies were not found in hamsters infected by the C⁺H⁰ variant. Interferon may have a role in tumor induction.

- 1520 IMMUNE RESPONSE TO GROSS VIRUS-INDUCED LYMPHOMA: I. KINETICS OF CYTOTOXIC ANTIBODY RESPONSE. (E.) Herberman, R. B. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.) and M. E. Oren. *J Nat Cancer Inst.* 46(2):391-396, 1971.

Male rats inoculated s.c. with cells from murine leukemias induced by Gross leukemia virus developed small tumors which regressed in 10-14 days in 65% of the cases; the remaining rats developed tumors which persisted for about 45 days before regressing. In rats with quickly-regressing tumors, the cytotoxic antibody response was found to describe a bimodal curve, with an early peak of mean antibody titer of 75 at 10 days postinoculation, and a second peak of mean titer of 650 at 30-40 days postinoculation. In the group of rats with more tenacious tumors, the first antibody peak occurred at 10 days postinoculation with a mean titer of 80; the second peak had a mean antibody titer of 820 and lasted from day 35-60 postinoculation. The height of the second antibody-titer peak in rats with enduring tumors was related to the size of the tumor-cell inoculum; large numbers of tumor cells elicited high titers of cytotoxic antibody. Rats given 1 x 10⁵ tumor cells developed mean antibody titers of 33, while rats given 5 x 10⁸ tumor cells developed antibody titers of 1280. Inoculation of a

second dose of tumor cells resulted in an increase antibody titers and the high titers persisted for 2 wk beyond the limit for control rats not given a second dose of cells. When antisera containing high titers of antibodies were fractionated on Sephadex G-200, the antibodies in initial-peak sera found to be 19S, and those in the second antibody titer peak were 7S.

- 1521 DIFFERENTIATION BY IMMUNOFERRITIN OF HERPES SIMPLEX VIRION ANTIGENS WITH THE OF RABBIT 7S AND 19S ANTIBODIES FROM EARLY (7-DAY) AND LATE (7-WEEK) IMMUNE SERA. (E.) Miyamoto, K. (Flow Lab., Rockville, Md.), C. Morgan, K. C. Hsu and B. Hampar. *J Nat Cancer Inst* 46(3):629-646, 1971.

Monolayer cultures of hamster kidney cells were infected with herpes simplex virus (HSV), and the interaction of the cells with HSV antibodies was studied. HSV antisera prepared in rabbits and fractionated by gel filtration into 7S and 19S fractions were separated into early and late antibodies, conjugated with ferritin and adsorbed with virus-infected hamster kidney cells. Before any virus appeared in the infected cultures, antigens which reacted with early 7S and 19S viral antibodies were found in the cytoplasm of infected cells and their nuclei, but most antigens which reacted with the late antibodies were found in nuclei only. Two hr after virus infection, ferritin-conjugated early 7S antibodies tagged small scattered aggregates of antigens in the cytoplasm. Large aggregates of antigens were found near the cell membrane or the nucleus 2-17 hr postinfection; these antigens reacted only with early 7S and 19S antibodies. There was evidence that disrupted nucleoli reacted with early 7S antibodies in the early stages of infection. Cytoplasmic antigens were thought to enter the nucleus through nuclear pores. In the nucleus, viral core of low density reacted with early 7S antibodies, while viral capsids reacted with both early 19S and late antibodies. Viral capsids were seen to be enveloped at the nuclear and tubular cytoplasmic membranes, the early stages of envelopment were marked by the appearance of "early" membrane-associated antigens which reacted with early 7S and late 19S antibodies. As envelopment progressed, the early membrane-associated antigens disappeared and antigens which reacted with early 19S and late 7S antibodies appeared. The antigenic sites on the viral capsid surface and envelope may differ in specificity for early 19S and late 7S antibodies.

- 1522 IMMUNOLOGIC MECHANISMS IN THE INDUCTION REGRESSION OF SHOPE PAPILLOMA VIRUS-INDUCED DERMAL PAPILLOMAS OF RATS. (E.) Kreider, J. W. (Med., Pennsylvania St. U., Hershey), S. A. Benjamin, Pruchnic and C. V. Strimlan. *J Invest Derm* 56(2):1971.

The effect of immunosuppressive therapy on the development and growth of epidermal papillomas induced by Shope papilloma virus was investigated in Lewis strain rats. Rats, which are normally resistant to Shope virus

induction, were treated with methylprednisolone (MP) or anti-rat lymphocyte serum, alone or together with thymectomy. The development and regression of tumors induced in MP-treated animals by grafts of virus-infected fetal rat tissue were observed. The incidence of papilloma development was increased 16-25% only by high (1.0 or 10.0 mg) doses of MP, compared to 0-8% in untreated controls. In untreated rats, papillomas regressed within 2 wk of appearance, while in MP-treated rats, tumors persisted until autopsy (6-8 wk). While mononuclear cell infiltration was observed to accompany tumor regression in controls, little infiltration was seen in rats treated with MP. The incidence of papilloma development in anti-lymphocyte serum-treated rats was not increased compared to untreated controls, nor did thymectomy affect the development of papillomas in rats given anti-lymphocyte serum. However, papillomas which developed in anti-lymphocyte serum-treated rats persisted to autopsy. An immunological mechanism apparently operates to cause papilloma regression in rats, while other factors seem to be involved in the original development of tumors.

- 1523 STUDY OF THE GROSS ANTIGEN IN BALB LEUKEMIAS AND TUMORS OF DIFFERENT ORIGIN.
(E.) Saal, F. (Natl. Acad. Med., Buenos Aires, Argentina), C. D. Pasqualini and S. L. Rabasa. *Cancer Res* 31(1):23-26, 1971.

Leukemias and other tumors of differing origins in BALB mice were investigated to detect the presence of Gross virus antigen (G). Leukemias were induced in the test mice by implantation of spontaneous leukemia cells from AKR mice and by implantation of tumor tissue induced by X-rays, ³²P, sarcoma 180, human leukemia tissue, and murine lymphoma tissue. All of the leukemias induced in BALB mice, whatever their origin, were G-negative when tested by the direct cytotoxic test. However, with the more sensitive indirect cytotoxic test or with typing by absorption, all leukemias and tumors of the BALB strain proved to be G-positive with the exception of Moloney leukemias. Cytotoxicity of the tumors was expressed as percent of stained, dead cells. At anti-G serum dilutions of 1/16, BALB mice showed high percentages of dead cells when inoculated with cells from normal BALB tissue (97%), spontaneous BALB leukemia (60%), and sarcoma 180 (71%). Lowest percentages of dead cells were found in mice given cells from leukemias induced by X-ray (8%), human leukemia (11%) and spontaneous AKR leukemia (10%). Leukemias and tumors of A and Rockland strain mice were G-negative. Syngeneic transplants of sarcoma 180 were G-positive in BALB mice and G-negative in Rockland mice. Normal AKR tissue increased in degree of G-positivity as the animals receiving implants increased in age. Apparently either the Gross virus or a relative of it is present in BALB mice in a latent state, becoming detectable upon the induction of leukemia or tumors by various inducing agents. The Gross virus, therefore, appears to have a role in malignant transformation consequent to the administration of an inducing agent.

- 1524 NEUTRALIZING ANTIBODIES TO SIMIAN VIRUS 40 (SV40) IN HUMAN SERA. (E.) Hahn, E. E. A. (Serafino Belfanti Milanese Sieroter. Inst., Italy). *Progr Immunobiol Stand* 3:44-47, 1969.

Laboratory workers having daily contact with monkeys were examined for neutralizing antibodies to SV40. Five persons who had contact with monkeys daily for periods of 4-6 hr donated serum samples which were found to be positive for SV40 antibodies, with titers ranging from 1:4-1:16. One veterinary worker with exposure to monkeys was antibody-negative. None of 20 sera taken from healthy blood donors without exposure to monkeys showed SV40 antibodies. Nineteen of these controls had been vaccinated with inactivated SALK polio vaccine. Apparently, SV40 had been transmitted from the monkeys to the animal handlers in the laboratory.

- 1525 PROPERTIES OF TRANSFORMED HAMSTER CELLS CONTAINING SV40 TUMOR ANTIGEN IN THE CYTOPLASM. (E.) Richardson, L. S. (Baylor Coll. Med., Houston, Tex.) and J. S. Butel. *Int J Cancer* 7(1):75-85, 1971.

The immune properties of transformed hamster cells containing SV40 tumor antigen in the cytoplasm were investigated. Eight transformed cell lines were established from tumors induced in 8 of 20 hamsters by hamster embryo fibroblasts which had been transformed *in vitro* by PARA-adenovirus 7. All of the tumor cell lines contained SV40 tumor antigens; in 6 of the 8 cell lines, antigen was contained in the cytoplasm exclusively, while in 2 lines antigen was found in nucleus and cytoplasm. All cell lines contained SV40 surface antigen; none contained adenovirus tumor antigen. Seven of 8 hamster sera contained SV40 tumor antibody; 3 serum samples produced adenovirus tumor antibody and 1 produced SV40 surface antibody. Tumor antigen remained localized in the cytoplasm in 5 of the 6 cell lines through 30 passages *in vitro*; antigen in the 6th cell line became localized in the nucleus after passage 23. Complement fixation tests and immunofluorescence tests successfully demonstrated cytoplasmic tumor antigen. When transformed cells containing cytoplasmic SV40 tumor antigen were transplanted *in vivo* to weanling hamsters, tumors developed in the majority of recipient animals with latencies of 2-9 wk. The transplanted cells contained SV40 tumor specific transplantation antigen.

- 1526 AMINO ACID PATTERN OF RIBONUCLEOPROTEIN AND PURIFIED T-ANTIGEN ISOLATED FROM HAMSTER TUMORS INDUCED BY ADENOVIRUS TYPE 12. (Rus.) Degtyarenko, V. I. (I. I. Mechnikov Sci. Res. Inst. Virol., Epidem., Odessa, U.S.S.R.), N. I. Zatsepin and A. V. Pertaya. *Biokhimiia* 35(6):1110-1112, 1970.

The amino acid composition of purified T-antigen and of the acid ribonucleoprotein isolated from adenovirus type 12-induced hamster tumors were found to have certain analogies. The contents of leucine, phenylalanine, valine, tyrosine, glutamic acid, threonine and serine were similar in both preparations. Differences were noticed in the contents of aspartic acid, glycine, histidine and aminobutyric acid. Tryptophan was not detected in the T-antigen protein but was present in the acid ribonucleoprotein. The T-antigen was composed of 22.7% of monoaminodicarboxylic acids, indicating it to be an acid protein. The highly lipophilic properties of the T-antigen were

considered to be due to its high content of aliphatic amino acids.

- 1527 THE "IMMUNOLOGIC DETERMINANTS" IN THE AVIAN ONCOGENIC VIRUS SYSTEM. PURIFICATION AND IMMUNOCHEMICAL CHARACTERIZATION OF THE ANTIGEN COMPLEX IN THE GROUP OF CHICK CELLS TRANSFORMED BY ROUS SARCOMA VIRUS (SCHMIDT-RUPPIN STRAIN). (Fr.) Rabotti, G. F. (Lab. Exp. Med. Coll. France, Paris) and B. Teutsch. *C R Acad Sci* 272(2):343-346, 1971.

The specific antigen of the avian sarcomas was shown to possess 4 distinct antigenic components: α_0 , α_1 , β and γ . By means of immunodiffusion and electrophoresis it was possible to separate out 3 distinct peaks: a double-peak in the area of gamma-globulin, another corresponding to beta-globulin and a third peak towards the anode. Three main active antigens appeared to be present in the antigen specific for the chick group, which were separable according to their molecular weight, the one with the highest molecular weight being double. After many trials, it was found that the most favorable chromatographic separation was with DEAE-Sephadex at pH 8.6 and that the α_0 and α_1 antigens could be eluted by the initial buffer, whereas β and γ were recovered in the fractions containing 0.02 to 0.1 M NaCl. A nomenclature is proposed on the basis of the antigenic activity.

- 1528 INTERFERON SYSTEM IN CELLS FROM HUMAN TUMORS AND FROM PERSONS PREDISPOSED TO CANCER. (E.) Worthington, M. (Natl. Inst. Allerg. Infect. Dis., Natl. Inst. Hlth., Bethesda, Md.) and S. A. Aaronson. *Infect Immun* 3(3):424-428, 1971.

The response of the interferon system in fibroblasts from persons predisposed to leukemia, fibroblasts from persons with neoplastic disease and in human tumor cells to polyinosinic-polycytidylic acid (poly I:C) and Chikungunya virus stimulation was evaluated. The minimal effective concentrations of poly I:C needed to induce resistance to Sindbis virus was 1 μ g/ml or less for all but one of the skin fibroblasts tested, while normal fibroblast cultures as well as lung, kidney, muscle and synovium showed complete suppression of Sindbis virus hemagglutination when treated with 10^{-4} dilution of Chikungunya virus. Cell lines derived from 4 sarcomas and 1 bronchogenic carcinoma were relatively resistant to the above poly I:C concentrations and Chikungunya virus dilution. However, at concentrations 10-100-fold greater, the Chikungunya virus was protective. The minimum effective concentration of human interferon for non-tumor cells was 5 U/ml or less, whereas 4 of the 5 tumors required concentrations of 50 U/ml, with the tumor most responsive to human interferon showing greatest sensitivity to the protective effects of both poly I:C and Chikungunya virus. The majority of tumor cells stimulated with heat-inactivated Chikungunya produced 30 U/ml or less of interferon in response to a 10^{-2} dilution of the virus, whereas nontumor cells produced at least 100 U/ml. Three of the tumor cell lines and 1 skin fibroblast strain

were found to contain mycoplasma contamination; however, these did not cause cells to become resistant to the antiviral effects of either poly I:C or interferon.

- 1529 IMMUNOSUPPRESSION BY LEUKEMIA VIRUSES: ULTRASTRUCTURAL STUDIES OF ANTIBODY-FORMING SPLEENS OF MICE INFECTED WITH FRIEND LEUKEMIA VIRUS. (E.) Koo, G. C. (Temple U. Sch. Med., Philadelphia, Pa.), W. S. Ceglowski and H. Friedman. *Immun* 106(3):799-814, 1971.

Male mice inoculated with infectious doses of Friend leukemia virus before being immunized with 0.5 ml a 10% sheep RBC suspension showed an impaired immune response to the sheep cells compared to mice infected with virus after immunization. Spleens of mice infected with virus 3 and 8 days before immunization had 95% and 98% fewer antibody plaque-forming cells than spleens of mice given sheep erythrocytes without virus infection. While mean serum antibody titers for uninfected, immunized mice and for mice immunized and infected on the same day were 7.0, 10.0 and 5.0, respectively, for mice infected 3 and 8 days before immunization were 5.0 and 4.0, respectively. The ultrastructure of spleens of uninfected, immunized mice was marked by abundant lymphoid cells and macrophages as well as plasmablasts. Spleens of mice infected with Friend virus 2 days before immunization were similar to spleens of uninfected mice; however, very few plasmablasts were seen in spleens of mice infected 3 days before immunization. Immature lymphoid cells and blast cells being the predominant cell types in these spleens. Immature neoplastic cells containing viral particles were so common in spleens infected before immunization. Infiltration of leukemic cells was even more pronounced in spleens of mice infected with virus 8 days before immunization with sheep red blood cells and virus particles were abundant. Plasma cells were not found in these spleens, and virus particles were seen budding from lymphocyte membranes. The results appear to be a competition between leukemia virus and antigen for common stem cells.

- 1530 IMMUNOLOGIC DEFICIENCY ASSOCIATED WITH MAMMARY TUMOR VIRUS (MTV) INFECTION IN MICE: HEMAGGLUTININ RESPONSE AND ALLOGRAFT SURVIVAL. (E) Blair, P. B. (Sept. Pact., Immun., U. California, Berkeley), M. L. Kripke, M. A. Lappe, R. Bonhag and L. Young. *J Immun* 106(2):364-370, 1971.

Female mice infected with mammary tumor virus (MTV) prior to immunization with sheep red blood cells showed lower mean hemagglutinin antibody titers than did immunized mice not infected with MTV. Immunized mice which were not infected produced high hemagglutinin titers (peaks at 9000-13000) 30 days after immunization with sheep erythrocytes. Six-month-old mice produced higher hemagglutinin titers than 8, 10 or 12-month-old mice. BALB/c mice developed higher mean titers than did BALB/cfC3H mice. Mice injected with MTV 4 days prior to immunization developed lower hemagglutinin titers than did uninfected mice; in both groups maximum titers were attained 5-7 days after immunization.

zation. Uninfected mice had mean hemagglutinin titers of 8.14 (\log_2 titer), while infected mice had mean titers of 5.29. Differences between infected- and uninfected-hemagglutinin titers were statistically significant only for serum samples collected from 7-month-old mice. Skin allografts survived longer on virus-infected mice than on uninfected mice. Immunologic deficiency was generally more pronounced in infected mice 10 months of age and older than in younger animals.

- 1531 IMMUNE RESPONSE TO GROSS VIRUS-INDUCED LYMPHOMA: II. KINETICS OF THE CELLULAR IMMUNE RESPONSE. (E.) Oren, M. E. (Yale-New Haven Hosp., Conn.), R. B. Herberman and T. G. Canty. *J Nat Cancer Inst* 46(3):621-628, 1971.

Subcutaneous inoculation of rats with 5×10^7 cells from a Gross virus-induced ascites lymphoma induced tumor nodules in 4 days which regressed by day 17; the cellular and humoral immune response of spleen cells to these tumor cells was investigated. Cellular cytotoxicity in mouse spleen cells, first noticeable on day 6 postinoculation, reached maximum values of 18% on day 10, and declined to near zero through day 50. Humoral antibody titers showed 2 peaks, the first occurring on day 10 (mean antibody titer of 55) and the second occurring on day 35 (mean titer of ~250); humoral antibody titers dropped to less than 10 between peaks. The height of the cellular immune response depended on the size of the initial dose of tumor cells and on the length of incubation time; cellular cytotoxicity for spleen cells of rats given doses with a spleen cell:tumor cell ratio of 50 was half that of spleen cells of rats given doses with a spleen cell:tumor cell ratio of 200. Spleen cells incubated for $1\frac{1}{2}$ hr had maximal cellular cytotoxic values which were less than a third those of spleen cells incubated for 4 hr. Increased cellular cytotoxicity could not be produced by inoculation of a second dose of tumor cells at 30-40 days after the initial inoculum.

- 1532 FLUORESCENCE COMPLEMENT FIXATION BY LYMPHOBLASTOID CELLS. (E.) Floyd, R. (Baylor Coll. Med., Houston, Tex.), V. Vonka and M. Benyesh-Melnick. *J Nat Cancer Inst* 46(2):383-390, 1971.

The presence and location of intracellular Epstein-Barr virus-soluble complement-fixing antigens were studied in 11 lymphoblastoid cell lines derived from normal individuals and from individuals with Burkitt lymphoma, infectious mononucleosis, acute myelogenous leukemia and acute lymphoblastic leukemia by means of fluorescence complement-fixation. Cells from the Burkitt lymphoma line possessed cytoplasmic fluorescence in 3-7% of cells, and nuclei were left unstained, while 10-12% of cells of the lymphoblastoid line obtained from an individual with infectious mononucleosis fixed complement in the absence of antiserum. All cells that fixed complement from the Burkitt lymphoma line possessed the Epstein-Barr virus, and 30-40% of the cells associated with mononucleosis were positive for the presence of the virus. All other cells tested gave negative results. One reason for the results noted could be the accumulation of

globulins produced by the cells or the presence of an antibody in the guinea pig serum used in the complement fixation test which was able to fix complement after forming an antigen-antibody complex with the antigen in the cell. However, this latter hypothesis is unlikely since guinea pig serum did not reveal any anti-Epstein Barr virus antibodies when followed with fluorescein-conjugated antiguinea-pig gamma globulin.

- 1533 CELL SURFACE ANTIGENS DETECTABLE BY CYTOTOXIC TEST ON FRIEND VIRUS-INDUCED AND FRIEND VIRUS-INFECTED TUMORS IN THE RAT. (E.) Shirai, T. (Hosp. Special Surg., New York, N. Y.), H. Kaji, N. Takeichi, F. Sendo, H. Saito, M. Hosokawa and H. Kobayashi. *J Nat Cancer Inst* 46(3):449-460, 1971.

The biological role of the antigen specified by Friend virus in relation to growth of tumors and its effect on other antigenic components of the cell surfaces of nonviral tumors were analyzed in rats of the Wistar-King-Aptekman, Wistar/Mk and Donryu strains by means of cytotoxic and quantitative absorption testing. Friend virus-induced rat tumors were distinguished by their growth rates following s.c. transplantations in which 2 failed to grow almost completely, and transplants of another grew to 20 mm average tumor diameter but ultimately regressed. A subline of this tumor resulted in lethal growth in normal adult Wistar-King-Aptekman rats. Cytotoxic effects of the Friend-specific antiserum were inversely related to growth rates *in vivo* for all tumor cell lines; Friend-virus infected cell lines were markedly sensitive to the antiserum. Rats that had resisted transplants of Friend virus-infected tumors acquired high transplantation resistance against syngeneic non-virus-infected tumors, and no cytotoxicity was demonstrated with other tumor cells to antiserum obtained from those rats.

- 1534 DEFECT IN CELLULAR IMMUNITY OF LEUKEMIA VIRUS-INFECTED MICE ASSESSED BY A MACROPHAGE MIGRATION-INHIBITION ASSAY. (E.) Friedman, H. (Temple U. Sch. Med., Philadelphia, Pa.) and W. S. Ceglowski. *Proc Soc Exp Biol Med* 136(1):154-158, 1971.

Cellular immunity of mice infected with Friend leukemia virus (FLV) was studied using an *in vitro* macrophage migration-inhibition assay to assess immunocompetence of mice to antigens of tubercle bacilli (PPD). Normal migration of peritoneal cells from nonleukemic mice immunized with Freund's complete adjuvant was readily inhibited *in vitro*. Addition of PPD to cell suspensions resulted in a significant decrease in the area of migration in the range of 40-60% with the inhibition reaction appearing maximally when the mice had been sensitized for 2-3 wk before sacrifice. The migration activity of peritoneal cells from both immunized and non-immunized FLV-infected mice was not inhibited by PPD. Rapid development of splenomegaly and blood cell dyscrasia culminating in erythroblastic leukemia was seen in FLV-infected mice. Failure to detect cellular immunity in FLV-infected mice correlates with the

marked decrease in humoral immunity previously assessed by skin graft rejection assays.

- 1535 IMMUNOSUPPRESSION BY LEUKEMIA VIRUSES:
VI. ULTRASTRUCTURE OF INDIVIDUAL ANTIBODY-
FORMING CELLS IN THE SPLEENS OF FRIEND LEUKEMIA
VIRUS-INFECTED MICE. (E.) Koo, G. C. (Temple U. Sch.
Med., Philadelphia, Pa.), W. S. Ceglowski, M. Higgins
and H. Friedman. *J Immunol* 106(3):815-830, 1971.

Typical murine leukemia virus particles were found in the plaque-forming cells (PFC) in spleens of mice infected with Friend leukemia virus 8 days before immunization with sheep RBC. Spleens of virus-infected and immunized mice contained 98% fewer PFC than spleens of mice immunized with sheep RBC but not inoculated with Friend virus. Plasma cells at various stages of maturity comprised all of the antibody-forming cells in the spleens of the latter group of mice; these plasma cells were either proplasmacytes (24%) or mature plasma cells (56%). About 20% of the PFC cells in the spleens of uninfected mice appeared to be degenerated with no structural organization to the nuclei. Sixty-four percent of the PFC from uninfected spleens contained virus-like intracisternal A-type particles; particles were found only in the intracisternal spaces of the endoplasmic reticulum of the plasma cells. The PFC of spleens of mice infected with Friend virus prior to immunization were comprised of proplasmacytes (10%) or mature plasma cells (60%); degenerated cells accounted for 20% of the PFC in these cells. Friend leukemia virus C type particles were found in 55% of these spleen cells, usually at the cytoplasmic membrane. These particles were larger than the particles seen in spleens from uninfected mice and were never found in the endoplasmic reticulum. Apparently, leukemia virus infection and antibody formation are not mutually exclusive processes at the level of the single spleen cell.

- 1536 DEMONSTRATION BY THE ANTIGLOBULIN CONSUMPTION TEST WITH MURINE ANTISERA OF COMMON ANTIGENS IN TISSUES INFECTED WITH THE MAMMARY TUMOR VIRUS FROM DIFFERENT MOUSE STRAINS. (E.) Holmes, E. C. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and D. L. Morton. *J Nat Cancer Inst* 46(2):253-260, 1971.

Mammary tumor virus antigens were prepared from tumors in mice known to contain this virus, and anti-mammary tumor virus antisera were prepared by injection of histoincompatible mammary tumors induced by the virus into mammary tumor virus-free mice. In an antiglobulin consumption test, antisera were reacted against tissues infected with the mammary tumor virus, and absorption of the anti-mammary tumor virus antibody by some virus-infected tissues was observed. It was found that mammary tumor virus prepared from tumors carried by mouse strains C3H/HeN, DD/He, DBA/2JN, A/He, RIII/An, and BALB/cf appeared to share a common antigen related to the mammary tumor virus.

- 1537 DIFFERENCES IN THE MANIFESTATION OF VIRUS SPECIFIC SURFACE ANTIGEN BETWEEN CELLS TRANSFORMED BY SV40 AND UV-IRRADIATED SV40. (E.) Klietmann, W. (Inst. Hyg., U. Freiburg, Germany) and N. Seemayer. *Int J Cancer* 7(1):50-58, 1971.

SV40 virus exposed to UV or inactivated by white light after photosensitization by toluidine-blue was not as antigenic as non-inactivated or control virus. Normal and transformed hamster cell lines were inoculated with inactivated or control SV40, and antigenic response to antisera prepared in hamsters by injecting them with varying amounts of SV40 was studied by the mixed hemagglutination reaction (MHA). SV40-specific surface antigen was demonstrated by MHA on hamster tumor cells induced by non-irradiated SV40. Hamster cells transformed by control SV40 were positive for both surface and tumor antigen of SV40; UV-irradiation of virus for 12 min produced a line of transformed cells of reduced infectivity by 5 log₁₀ steps and diminished the surface antigen response. Other cells transformed by UV-irradiated SV40 were negative or showed a strongly diminished tumor antigen response and a diminished surface antigen response. The infectivity of cells transformed by photosensitized and white-light exposed SV40 were positive for tumor antigen and showed diminished SV40 surface antigen response. Cell lines induced by control SV40 yielded positive antigenic reactions up to anti-serum dilutions of 1:12; however, cells transformed by SV40 inactivated by UV or by white light only gave positive results in MHA at antiserum dilutions of 1:80 and 1:160, respectively. After 3 inoculations into adult hamsters, control SV40 induced a specific transplantation resistance to SV40-transformed tumor cells which fully protected the recipient hamsters from tumor development. Hamsters immunized with UV-irradiated SV40 developed tumors in more than 50% of the cases. All cell lines with diminished surface antigen caused malignant tumors when inoculated into adult hamsters.

- 1538 THE USE OF AN *IN VITRO* TEST FOR THE ESTIMATION OF PRESENCE OF THE SPECIFIC TUMOR ANTIGEN OF THE TRANSPLANTATION TYPE INDUCED BY SV40 VIRUS. (E.) Pekarek, J. (Res. Inst. Immun., Prague, Czechoslovakia), J. Svejcar, V. Vonka and H. Zavadil. *Progr Immunobiol Stand* 3:365-368, 1969.

Changes in the migration activity of cells of mesenchymal origin as a reaction specific for delayed hypersensitivity following infection with simian virus 40 were studied by means of spleen fragment cultivation. Migration activity of spleen cells from hamsters made resistant to the transplantation of tumor cells was considerably inhibited during cultivation in the presence of transformed cells; in the presence of normal cells their migration activity was comparable to that of control hamsters. Secondary green monkey kidney cell cultures infected with simian virus 40 and spleen fragments from either infected or non-infected cells of control hamsters was not substantially influenced, but inhibition of migration was observed with spleen cells of resistant hamsters.

hamsters in the presence of infected cell monolayers; its rate was dependent on the period after infection, and the most marked results were seen in cultures infected 24 hr prior to addition of the fragments. These results seem to demonstrate the presence of the surface antigen of simian virus 40 transformed cells in cell cultures undergoing a cytolytic infection.

1539 MALIGNANT LYMPHOMAS AND PLASMACYTOSIS IN MICE UNDER PROLONGED IMMUNOSUPPRESSION AND PERSISTENT ANTIGENIC STIMULATION. (E) Krueger, G. R. F. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), R. A. Malmgren and C. W. Berard. *Transplantation* 11(2):138-144, 1971.

Mice of 2 strains (BALB/c and C57B1) were given immunosuppressive treatment by azathioprine (15 mg/kg/day), or antilymphocyte serum (ALS, 0.25 ml) and antigenic stimulation by i.p. injections of lactic dehydrogenase virus (LDV), Freund's adjuvant (0.05 ml doses), viable HeLa cells, or vaccination with smallpox vaccine. Control mice went untreated or were given either antigenic stimulation or immunosuppressive treatment alone. Hyperplasia in lymphoreticular tissue was seen in all mice, control as well as experimental, except mice given LDV and ALS and untreated controls. Mice given antigenic stimulation alone, of whatever type, showed secondary follicles, plasma cell differentiation in the medullary cords, and activation and pyroninophilia of reticulum cells in the perifollicular area. Mice on azathioprine treatment alone showed depletion of the small lymphocytes from lymph nodes and spleen. Mice on ALS treatment alone showed small lymphocyte depletion and an increase of plasma cells in the medullary cords of lymph nodes. Malignant lymphoblastic lymphomas developed in 20% of BALB/c mice given azathioprine and antigens. No control mice developed lymphomas. Forty percent of BALB/c mice and 27% of C57B1 mice given ALS, with or without antigens, developed immature plasmacytoses; chronic treatment with ALS led to membrane glomerulitis and glomerulonephrosis in 8% of ALS-treated mice. Mice given antigens in addition to chronic ALS treatment showed the most severe glomerulonephrosis. Circulating antigen-antibody complexes were thought to cause the kidney lesions, and the lymphomas were seen as a result of antigenic stimulation under immunosuppressed conditions.

1540 IMMUNOSUPPRESSION BY ANTILYMPHOCYTE SERUM AND ITS EFFECT ON TUMORS INDUCED BY 3-METHYLCHOLANTHRENE IN MICE. (E.) Wagner, J. L. (Sch. Med. U. North Carolina, Chapel Hill) and G. Haughton. *J Nat Cancer Inst* 46(1):1-10, 1971.

The effect of prolonged diminution of, or abrogation of, the graft rejection response by heterologous antilymphocyte serum (ALS) on the incidence and latency of tumors induced by a standard dose of chemical carcinogen (0.25-0.50 mg of 3-methylcholanthrene, MCA) was tested in mice of both sexes. Seventy-three percent of the mice injected with (ALS) 50 days after injection of MCA and surviving after 400 days developed tumors compared to 78% of the

control group which received no ALS. However, only 9% of those injected with ALS survived in comparison to 15% of the control group, and metastases occurred in 27% and 19%, resp. Of 68 mice treated with ALS on the day of MCA administration, only 1 animal failed to develop tumors compared to 5 of 88 of the control group. Over a 12-week period more ALS-treated mice died with tumors than did mice injected with carcinogen only or control groups receiving nothing. After 152 days, 46 of 50 mice treated with ALS and 45 of 50 mice treated with carcinogen had palpable tumor with no difference either in latency or in total incidence of MCA-induced tumors. The death rate in mice receiving a standard dose of MCA and treated with immunosuppressant did not differ from the group receiving carcinogen alone. The immune response which can be suppressed with ALS is largely ineffectual in preventing the appearance of primary neoplasms induced by injection in mice of 250 to 500 µg of MCA; however, the graft rejection response was suppressed by ALS for at least 84 days.

1541 THE EFFECT OF ANTILYMPHOCYTE SERUM ON EXPERIMENTAL HAMSTER BUCCAL POUCH CARCINOGENESIS. (E.) Giunta, J. L. (Tufts U. Sch. Dent. Med., Boston, Mass.) and G. Shklar. *Oral Surg* 31(3):344-353, 1971.

The effect of systemically injected anti-hamster lymphocyte serum (ALS) on 7,12-dimethylbenz(a)anthracene (DMBA)-induced epidermoid carcinogenesis of the buccal pouch has been studied in male and female Syrian hamsters through cytologic analysis. Painting with DMBA resulted in a generalized whitened, granular surface interspersed with erythematous areas, and tumor masses which were well-defined raised papillary and nodular lesions with some ulceration and hemorrhage. ALS/DMBA pouches appeared to present lesions at earlier stages than those of the DMBA group with more extensively altered areas showing patterns of dyskeratosis and frank carcinoma alternately. Many anaplastic lesions appeared in the ALS/DMBA group compared to solitary ones among the DMBA group. Spleens in the ALS/DMBA group had a disorganized architecture with scanty lymphatic nodules as well as sinusoids engorged with lymphocytes and erythrocytes, whereas the DMBA control group had essentially normal spleens. Lymph nodes in the DMBA group were slightly to moderately enlarged with prominent germinal follicles and dilated central sinusoids, whereas the ALS/DMBA group gave evidence of normal or slightly enlarged nodes with consistently sparse germinal follicles. However, at later periods nodes in the latter group became moderately to severely enlarged with disorganized architecture obliterated by a proliferation of "blast" type cells throughout. No metastases were found in either experimental group at the termination of the experiment at 16 wk.

1542 HL-A ANTIGENIC LOSS IN MALIGNANT TRANSFORMATION. (E.) Seigler, H. F. (Duke U. Med. Ctr., Durham, N. C.), W. B. Kremer, R. S. Metzgar, F. E. Ward, A. T. Haug and D. B. Amos. *J Nat Cancer Inst* 46(3):577-584, 1971.

In vitro isoantigenic changes of antigens were studied in the peripheral lymphocytes of a patient with malignant lymphoma. Cytotoxicity reactions with HL-A antiserum were negative for HL-A antigens on the lymphocyte specified by the patient's genotype as the malignant lymphoma with normal peripheral lymphocytes progressed to disease with circulating neoplastic lymphocytes. Absorption of 3 positively reacting antisera with abnormal lymphocytes from the patient failed to remove their cytotoxicity, whereas cells from the HL-A identical sibling lost all cytotoxic activity. Skin fibroblasts demonstrated the same serologic reaction pattern as the initial typing on the peripheral lymphocytes, indicating that the patient's membrane-associated isoantigens remained unaltered, while the malignant lymphoid cells demonstrated a loss of reactivity with HL-A antisera. In response to phytohemagglutinin, lymphocytes obtained at the time of remission showed a low uptake of precursors while the abnormal cells obtained when the disease was again active gave evidence of increased incorporation of precursors into RNA, DNA, and protein synthesis with a decline in synthetic capability after 72 hr.

- 1543 EFFECTS OF ANTILYMPHOCYTE SERUM (ALS) ON THE INDUCTION OF LYMPHOCYTIC LEUKEMIA IN MICE. (E.) Law, L. W. (Natl. Cancer Inst., Natl. Inst. Hlth, Bethesda, Md.) and S. S. Chang. *Proc Soc Exp Biol Med* 136(2):420-425, 1971.

The relationship between immunologic reactivity, using antilymphocyte serum as an immunosuppressant, and the induction and repression of lymphocytic neoplasms in adult BALB/c mice infected with murine leukemogenic virus was studied by determining virus and virus neutralizing antibody titers. Twelve-week old animals resisted the leukemogenic effect of the i.p. injection of murine leukemia virus compared to those receiving antilymphocyte serum in which lymphocytic leukemia was detected as early as 1.5 months after infection with death following within 2 wk. Antilymphocyte serum alone was ineffective, and normal rabbit serum was previously observed not to influence murine leukemia virus induction of lymphocytic leukemia. However, an unexpected finding was the lack of response to the leukemogenic effects of the virus in antilymphocyte serum-treated animals 6-8.5 months of age at the beginning of treatment in 15 mice. Reversal of susceptibility in serum-treated animals by adoptive transfer of syngeneic adult normal lymphoid cells was accomplished and probably represents replacement of those immune elements removed by the antilymphocyte serum.

- 1544 REAPPEARANCE AND RELATIVE IMPORTANCE OF IMMUNOCOMPETENT CELLS IN THE THYMUS, SPLEEN AND LYMPH NODES FOLLOWING LETHAL X-IRRADIATION AND BONE MARROW RECONSTITUTION IN MICE. (E.) Blomgren, H. (Karolinska Inst., Stockholm, Sweden) and B. Andersson. *J Immunol* 106(3):831-834, 1971.

The reappearance of immunologic competence in 1-month-old (A.CA x C57BL) F_1 hybrid mice following lethal X-irradiation and bone marrow reconstitution were followed at the whole animal level and in various lymphoid

cell populations. Groups of mice injected with sheep erythrocytes showed peak antibody titers from 2.7 to 4.0 log₁₀ on day 6 in unirradiated animals used as controls, and slightly enhanced response was noted in irradiated mice given 10⁷ thymus cells. In irradiated mice, mice challenged on day 0, with sheep erythrocytes showed no response, and peak titers were obtained on day 20; enhancement of response was seen in animals receiving thymic cells along with the erythrocytes. As the time of immunization after irradiation was increased from 0 to 25 days in irradiated mice injected with or without thymic cells, recovery progressively increased to give peak titers ranging from 0.00 for the spleen on day 14 to 3.10 for thymus cells on day 25. Thymus-dependent lymphocytes, although not known to produce humoral antibodies themselves, seem to enhance antibody formation against certain antigens. Origin of these cells is not known.

- 1545 *IN VITRO* ASSAY OF CELL MEDIATED IMMUNITY IN HUMAN CANCER: DEFINITION OF LEUKOCYTE MIGRATION INHIBITORY FACTOR. (E.) Wolberg, W. H. (U. Wisconsin Med. Sch., Madison) and M. L. Goelzer. *Nature* 229(5287):632-634, 1971.

The migration of leukocytes incubated with human tumor cells was investigated in order to elucidate the diminution of the cutaneous hypersensitivity response to tumor cells obtained from breast carcinomas, bronchogenic carcinomas, and other tumors. When tumor cells were incubated with the patient's leukocytes, it appeared that the tumor cells liberated a substance which inhibited migration of the leukocytes by as much as 79% in some preparations. The addition of phytohemagglutinin to the preparation also inhibited leukocyte migration. Partial reversal of this inhibition occurred when blastogenesis was blocked by 5-fluorodeoxyuridine in concentrations greater than 1 x 10⁻⁷M. Human tumors apparently contain or produce a substance which inhibits *in vitro* migration of leukocytes obtained from the individual in whom the tumor arose. This substance may adversely affect the defensive delayed hypersensitivity reaction in the host.

- 1546 CELL CULTURE OF THREE ANTIBODY-PRODUCING MURINE PLASMACYTOMAS. (E.) Periman, P. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *J Nat Cancer Inst* 46(2):403-410, 1971.

Plasmacytomas originally induced by mineral oil injections in mice were maintained as 3 cell lines *in vitro* for as long as 24 months in one case. All 3 cell lines were composed largely of mononuclear round cells having prominent Golgi apparatus, and many free ribosomal particles and extensive rough endoplasmic reticulum. Numerous intracisternal A-type particles with 2 electron-dense membranes and a lucent center were found in the rough endoplasmic reticulum. When viable cells from the 3 lines were injected s.c. in mice, plasma cell tumors resulted which secreted immunoglobulins with the same antibody activity as those produced by the original tumor; light chain was found by immunodiffusion in the urine of mice bearing tumors produced by cell culture inocula. The cell lines maintained

in vitro also produced immunoglobulins antigenically similar to those produced by the parent tumors, and also secreted the same types of light and heavy chains which were secreted by parent tumors.

- 1547 COMPARISON OF ACTIVE AND ADOPTIVE IMMUNITY INDUCED BY A CONGENITAL MOUSE TUMOR. (Fr.) Oth, D. (Fac. Sci. Nancy, France), M. Bujadoux and C. Burg. *C R Soc Biol* 164(5):1104-1108, 1970.

Experiments are described in which immunization of mice with congenital tumors (C57Br) was carried out by the transfer of about 10^8 immunocompetent cells taken from animals previously immunized against this tumor. The number of cells injected was far less than the total immunocompetent cells present in the donor animal, and it was assumed that the adoptive immunity would be less than that of the active immunity normally obtained. The results, however, revealed that the actively immunized animals were less immune to tumor transplantation than the ones immunized adoptively when calculated in terms of survival. This result may be explainable on the basis that at the time of the inoculation of the viable tumor, the number of immunocompetent cells immunized against the tumoral neoantigens was greater in the adoptive immunity group than in the active immunity group. In the present study, the immunocompetent cells sensitized against specific tumoral antigens may have multiplied more quickly than the others when transferred to nonimmunized animals. Regulator feed-back mechanisms in the synthesis of antibodies are discussed.

- 1548 THE CELL SITE OF THE IMMUNOLOGICAL DEFECT IN TUMOR-BEARING MICE. (E.) Bianco, G. (Harvard Med. Sch., Boston, Mass.), B. L. Brown, E. E. Jones and V. M. Rosenoer. *Proc Soc Exp Biol Med* 136(2):507-509, 1971.

Observation of the primary immune response in mice bearing implants of the Ridgeway osteogenic sarcoma indicated that when the tumor was far advanced, the capacity of host spleen cells to respond to injections of sheep erythrocytes was impaired; when the tumor weighed 3 g the number of plaques/spleen was 36% of control values, and 1 day later the number of plaques was 5% of control. Normal mice given injections of sheep RBC showed slight splenic enlargement and some increase in mitotic figures; mice bearing sarcomas had striking splenomegaly and prominent mitotic figures. Sarcoma bearing mice injected with sheep erythrocytes showed similar splenic changes, but the degree of the changes was more advanced. Apparently, the major process resulting in splenomegaly in tumor-bearing mice was hyperplasia, acting predominantly in the lymphoid cells. In *in vitro* experiments, spleen cells of mice were treated to separate macrophage cells and lymphocytes, and the macrophage cells from tumor-bearing mice were combined with normal lymphocytes or with lymphocytes from the tumor-bearing mice which were the source of the macrophage cells. Lymphocytes from tumor-bearing mice produced fewer plaques when incubated with macrophage from control mice than lymphocytes

from control animals incubated under similar conditions. Macrophage cells from tumor-bearing animals behaved normally when combined with control lymphocytes, suggesting that the immune defect in tumor-bearing mice was located in the lymphocyte cell population of spleen cells.

- 1549 ISOLATION OF METH A CELL SURFACE MEMBRANES POSSESSING TUMOR-SPECIFIC TRANSPLANTATION ANTIGEN ACTIVITY. (E.) McCollister, D. L. (Francis Delafield Hosp., New York, N. Y.). *Cancer Res* 30(12):2832-2840, 1970.

A method is described for the isolation of surface membranes from transplanted Meth A ascites tumor cells in BALB/c mice and leukemic cells of AKR/J mice and the detection of tumor-specific transplantation antigen activity through centrifugation and phase and electron microscopy. The isolation of surface membrane ghosts appeared to depend upon the borate present in the harvesting solution; the process was followed microscopically, showing final pellets of both types of cells to be white, and under phase microscopy showed slight swelling of the cell, Brownian movement of intracellular particles and, finally, a bursting of the cell with or without expulsion of the nucleus. Completely detached membrane ghosts were recovered and appeared as structureless bags offering very little contrast, especially where free of all visible structures, with greatest contrast appearing at the periphery or where the membrane was folded or torn. Under electron microscopy linear elements with trilamellar structures typical of biological membranes about 80 Å thick and devoid of mitochondria and nuclei were observed. Estimates made from counts on recovered ghosts and the number of whole cells just prior to extraction indicated that ghosts were recovered from 10-50% of the Meth A cells and 50-70% of the AKR/J leukemic cells (1 ml of packed Meth A cells yielded about 0.73 mg of lyophilized material in isolated ghost fraction). Ghosts of both types of cells may be transformed to a microscopically invisible state by 20 forceful passages with a syringe through a No. 21 needle. Female mice immunized with either Meth A or AKR/J leukemic cell membrane suspensions or disrupted Meth A ghosts and subsequently challenged with freshly harvested, viable Meth A cells showed a mean survival time of 17.1 to 21.2 with the higher rate among those immunized with disrupted Meth A ghosts. The number of animals surviving a 60 or 80-day period ranged from 0/10 to 10/12 with the highest incidence of survival appearing among animals treated with higher concentrations of either whole or disrupted Meth A ghosts. Whether or not true tumor-specific transplantation antigen activity is associated with surface membrane ghosts needs clarification with experimentation with autochthonous tumors.

- 1550 DEMONSTRATION BY COLONY INHIBITION METHODS OF CELLULAR AND HUMORAL IMMUNE REACTIONS TO TUMOR-SPECIFIC ANTIGENS ASSOCIATED WITH AMINOAZO-DYE-INDUCED RAT HEPATOMAS. (E.) Baldwin, R. W. (Cancer Campaign Res. Lab., U. Nottingham, England) and M. J. Embleton. *Int J Cancer* 7(1):17-25, 1971.

Hepatomas were induced in rats by p.o. administration of 4-dimethylaminoazobenzene; tumor cells were inactivated by exposure to 15,000 r of X-irradiation, and then were used to immunize rats against hepatoma transplants. Implantation of irradiated hepatoma cells caused immunized rats to reject tumor cell challenges in 100% of cases. Lymph node cells from immunized rats were incubated with hepatoma cells, with the result that in 15 of 17 colony-inhibition tests, lymph nodes from immune rats inhibited colony formation by tumor cells; reductions in colony formation ranged from 20-79%. That the colony-inhibition by lymph nodes was specific for the rat hepatoma against which lymph node donor rats had been immunized, was shown by the fact that lymph node cells from immunized mice failed to inhibit colony formation by cells of 10 tumors other than those of the original hepatoma. In similar tests, lymph nodes inhibited colony formation by target tumor cells only. Serum from tumor-immunized rats inhibited colony formation by target tumor cells, colony inhibition values ranging from 29-94%; the serum was inhibitory only against tumor cells against which the serum-donor rat had been immunized.

- 1551 INHIBITION OF IMMUNE RESPONSE AFTER TUMOR TRANSPLANTATION AND CHEMICAL CARCINOGENESIS IN MICE. (E.) Gericke, D. (Farbwerke Hoechst AG, Frankfurt, Germany), P. Chandra and A. Wacker. *Z Krebsforsch* 75(2):85-89, 1971.

Mice injected s.c. with 3-methylcholanthrene (MC, 0.05 mg/20 g body wt) were given an immunizing dose of sheep erythrocytes 7-77 days after inoculation to study the immune responses of the mice at intervals after methylcholanthrene treatment. An inhibition of plaque formation was seen 1 wk after treatment with MC; the serum plaque titers were half that of normal mice not given carcinogen. No significant inhibition of immune response was seen in treated animals 2 wk after treatment. Serum plaque formation after 0.02 mg/20 g MC remained in a suppressed state for 5 wk after treatment; twenty wk later when 3 of 6 mice had developed tumors, plaque forming cells were significantly reduced (67% of control). In another series of experiments, the immunological response after tumor transplantation was examined. Twenty-four or 48 hr after tumor transplantation, mice were injected with sheep red blood cells; inhibition of immune response was observed 48 hr after tumor transplantation, and inhibition was maximal in mice implanted with sarcoma-180, and less pronounced in melanoma. Though the immunosuppressive effects of MC were confirmed, the results did not force the conclusion that this immunosuppressive action was responsible for chemical carcinogenesis.

- 1552 RESISTANCE TO TRANSPLANTS OF RECENT SPONTANEOUS PARENTAL LINE TUMORS BY F₁ HYBRID HOSTS. (E.) Sanford, B. H. (Massachusetts Gen. Hosp., Boston) and S. F. Soo. *J Nat Cancer Inst* 46(1):95-101, 1971.

The basis for the greater resistance of F₁ hybrid hosts to strain-specific tumors was studied in experiments utilizing A/HeHa and C3H/StHa mice. F₁

hybrid hosts showed significantly increased resistance to parental tumor lines A-4, A-5, and C-9 with no difference in resistance noted in A-10 tumors; no significant sex differences were noted. Immunosuppression of the F₁ hosts by thymectomy plus irradiation significantly decreased the resistance to the A-4 and A-5 lines, while pretreatment with killed *M. tuberculosis* increased the resistance of F₁ mice. Testing the C3H lymphoma C-9, differences in response between syngeneic and F₁ hosts were found only at dosage of 5000 cells with no susceptibility shown in F₁ recipients, while 22 of 24 syngeneic hosts developed tumors. Resistance of F₁ mice could be completely abolished by immunosuppression, with all thymectomized irradiated F₁ mice developing tumors within 30 days. With ascites mammary adenocarcinoma A-10, both syngeneic and F₁ hosts reacted similarly to a variety of dosages with ascites forming by 30 days after inoculation, whereas all animals of the allogeneic C3H strain were resistant. A tumor-specific antigen of unknown nature is possibly involved here.

- 1553 IMMUNIZATION SCHEDULES FOR POTENT RABBIT ANTISERA TO LEUKEMIA L1210. (E.) Kim, C. A. H. (Tufts U. Sch. Med., Boston, Mass.) and A. E. Reif. *Cancer Res* 31(1):7-11, 1971.

The immune response which results in the production of antisera in rabbits immunized with cells of mouse leukemia L1210 cells was studied in animals given inocula of whole and disrupted cells of varying sizes and on differing schedules. Three animals were given i.v. injections of 30 million leukemia cells followed 50, 87, 89, 99, 101, 106 and 108 days later by reinoculations of the same dose. Antisera were separated into γ M and γ G fractions by gradient ultracentrifugation; γ M and γ G fractions comprised nearly the whole antiserum. The first inoculation produced a classical immune response; γ M antibody was first detected on day 4 postinoculation and showed a cytolytic potency (100/cytolytic titer) of 15, while γ G was first detected on day 8 at a cytolytic potency of 12. γ M reached maximum values on day 6 with a cytolytic potency of 8, and thereafter declined to a cytolytic potency of 8, and thereafter declined to reached maximum levels of potency (60) on day 12 and declined to a potency of (18) on day 50. Secondary immunization on day 50 and on following immunizations produced maximum potency of 35 for γ M antibody but increased the potency of γ G to 700. Subsequent immunizations increased γ G levels to 2000 by day 50 but produced diminishing γ M responses. Repeated inoculations with large doses of whole leukemia cells produced highly potent cytolytic antisera more effectively over time than did i.m. inoculation or inoculation with homogenized cells, sonically disrupted cells, or whole cells in addition to Freund-McDermott adjuvant. When reimmunization was protracted at length, evidence of immune exhaustion began to appear.

- 1554 BLOCKING EFFECT OF SERUM FROM TUMOR-BEARING ANIMALS ON MACROPHAGE MIGRATION INHIBITION WITH TUMOR ANTIGENS. (E.) Halliday, W. J. (Dept. Path., U. Washington, Seattle). *J Immunol* 106(3):855-857, 1971.

Macrophage migration from capillary tubes containing peritoneal cells drawn from mice was inhibited by extracts obtained from sarcomas induced in mice by Moloney sarcoma virus or methylcholanthrene. Peritoneal cells were prepared from mice after the regression of sarcomas induced in them by Moloney virus or after removal of tumors induced by methylcholanthrene. The peritoneal cells were incubated with tumor extracts and with serum prepared from mice with virus- or carcinogen-induced tumors. Macrophage migration was measured as the mean area of magnified migration from the capillary tube. The extract from Moloney virus-induced tumors failed to inhibit the migration of macrophage from peritoneal cells taken from mice with methylcholanthrene-induced tumors, but extracts of methylcholanthrene-induced tumors did inhibit the migration of macrophages from these peritoneal cells. Specificity of the inducing agent was also found for macrophage migration inhibition by sera from virus-induced tumor bearing mice.

- 1555 ABROGATION OF PASSIVELY TRANSFERRED TUMOR IMMUNITY *IN VIVO* BY ANTIGENICALLY RELATED TUMOR CELLS. (E.) Wepsic, H. T. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), I. D. Bernstein, B. Zbar, T. Borsos and H. J. Rapp. *J Nat Cancer Inst* 46(1):195-202, 1971.

The ability to establish passive tumor immunity was studied through systemic transfer of ascitic tumor cells from primary hepatomas in syngeneic Sewall-Wright strain-2 male guinea pigs by transfusion of peritoneal exudate (PE) cells. The ascites line-1 tumor cells in the peritoneal cavity significantly abrogated the transfer of tumor-specific immunity. In animals receiving PE cells but no tumor cells, the 7-day papule growth was $0.4 \pm 0.4 \text{ mm}^2$ following a challenge with an intradermal injection of live ascites tumor cells; in those animals which were given tumor cells 24 hr before the transfer of PE cells papule growth was similar to that of controls receiving tumor cells and was $11.0 \pm 1.6 \text{ mm}^2$. The transfer of tumor immunity was partially inhibited by the i.p. injection of ascites line-1 tumor cells before transfer but was not significantly altered by ascites line-7 cells; when ascites tumor cells were given on the same day as the transfusion with PE cells and challenged with ascites line-1 tumor cells 24 hr after transfusion of PE cells, suppression of growth of the intradermal tumor resulted. Intradermal papules did not grow in transfused, tumor-free animals, and X-irradiated line-7 cells injected i.p. had no effect on the transfer of line-1 tumor immunity. Injection (intracutaneous) of 1×10^9 X-irradiated line-1 ascites tumor cells inhibited the transfer of line-1 tumor immunity, and tumor cells mixed *in vitro* with PE cells inhibited the transfer of tumor immunity with no significant alteration in growth. Specific immunologic interaction between tumor cells and specifically sensitized cells probably accounts for survival of tumors in the face of an immune response in the host.

- 1556 THE EFFECT OF "EXOGENOUS" RNA ON THE IMPROVEMENT OF SYNGENEIC TUMOR IMMUNITY. (E.) Rigby, P. G. (U. Nebraska Coll. Med., Omaha). *Cancer Res* 31(1):4-6, 1971.

The effect of exogenous RNA treatment on survival of injected tumor cells was investigated in mice given s.c. or i.p. injections of syngeneic tumor cells and injected with RNA prepared from yeast at various times relative to tumor challenge following immunization with irradiated tumor cells. Controls given only live tumor cells had a mean survival of 19.5 days; immunization with irradiated tumor cells followed by tumor challenge produced a mean survival of 21.9 days, a difference which was not statistically significant. RNA alone, administered every other day for the 14 days before live tumor challenge or every other day for the 14 days after live tumor challenge, produced no appreciable change in mean survival times. However, when RNA was combined with the 2 doses of irradiated tumor cells and administered on day 7 and day 14 after tumor cell challenge, the mean survival time increased to 24.5 days, a statistically significant increase. When immunized mice were given RNA every other day after live tumor cell challenge, survival reached 36.1 days. The irradiated cells apparently prompted antigenic recognition in the recipients so that after live tumor cell challenge, the yeast RNA was able to produce an effective immune response to the tumor.

- 1557 EFFECT OF NORMAL TISSUE RIBONUCLEIC ACID ON A MURINE LEUKEMIC TRANSPLANT. (E.) Colmerauer, M. E. M. (Natl. Acad. Med., Buenos Aires, Argentina), C. Dosne Pasqualini and S. L. Rabasa. *Medicine* 30(5):447-450, 1970.

Mice were given i.p. injections of RNA prepared from normal mouse spleen or liver in amounts of 0.5 or 3.0 mg followed by challenge with 40 leukemia cells; RNA injections rendered mice more receptive to the leukemia cell transplant. Of 28 mice given liver RNA and challenged with tumor cells, all died within 17 days; of 30 mice given tumor cells but no RNA treatment, 14 survived, while mice which died survived for 24 days. Although 14 of 35 challenged mice treated with spleen RNA survived, there probably is no significant organ-specific difference between the transplant receptivity of mice treated with spleen RNA and that of mice treated with liver RNA. RNA apparently has an immunosuppressive effect in the mouse leukemia transplant test system.

- 1558 PROLONGED SURVIVAL OF MALE-TO-FEMALE SKIN ISOGRAFTS AND OF ALLOGRAFTS FROM NORMAL MICE FOLLOWING TREATMENT OF RECIPIENT OR GRAFT WITH SERA FROM TUMOR-BEARING MICE. (E.) Wexler, M. R. (Hebrew U. Hadassah Med. Sch., Jerusalem, Israel), M. Kripke and D. W. Weiss. *Cancer Res* 31(2):122-126, 1971.

The survival time of skin allografts derived from normal male mice and tumor-bearing mice was studied in female mice following treatment of the recipient or the graft with sera from males carrying lymphosarcoma. Skin grafts derived from donors carrying the transplanted lymphosarcoma for 24-35 days survived longer than similar grafts from normal animals or from those carrying the tumor for shorter or longer periods of time. In several instances, tumors developed at the graft sites in the recip-

ient animals or immediately adjacent to the area. Pretreatment of either the graft hosts or of the grafts with serum derived from isogenic animals carrying an implanted lymphosarcoma for 1-3 wk significantly prolonged the life of normal male skin isografts in female recipients, whereas serum obtained from animals carrying the tumor 4-5 wk was ineffective for pretreatment of graft hosts but was effective for graft incubation. Treatment of hosts with sera from tumor-bearing animals did not lead to a statistically significant shortening of the life of the graft under any of the experimental conditions used.

- 1559 QUANTITATIVE ASSESSMENT OF CELLULAR AND HUMORAL RESPONSES TO SKIN AND TUMOR ALLOGRAFTS. (E.) Canty, T. G. (Massachusetts Gen. Hosp., Boston) and J. R. Wunderlich. *Transplantation* 11(2): 111-116, 1971.

The relation between the humoral and cellular responses in the homograft reaction was studied in different lymphoid populations following skin and intraperitoneal tumor allografting across a strong histocompatibility barrier in normal and antilymphocyte-serum-suppressed adult BALB/c mice. Cellular immune activity was highest in the regional lymph nodes during the 1st wk following the challenge by skin allograft, while intraperitoneal challenge with tumor cells resulted in peak activity in the spleen and mesenteric lymph nodes. Skin graft survival times for animals pretreated with antilymphocyte serum averaged 19 days compared to 10 days for control animals receiving no treatment. Selective inhibition of cellular vs humoral immune responses in animals given a standard immunosuppressive dose of antilymphocyte serum was not demonstrable.

- 1560 INFLUENCE OF L-ASPARAGINASE ON ANTIBODY PRODUCTION AND GROWTH OF TUMORS IN ALLOGENEIC MICE. (E.) Miura, M. (Nagoya U. Sch. Med., Japan), K. Kawashima, T. Uetani, M. Hirano, H. Kakizawa, R. Ohno, A. Morita, H. Nishiwaki and K. Yamada. *Cancer Res* 31(2):114-121, 1971.

The effect of L-asparaginase on immunosuppression in several strains of mice was studied by measuring the change in production of circulating antibodies against sheep erythrocytes and allogeneic tumor cells and the incidence of ascitic leukemic tumor take in the allogeneic mice. Inhibition of primary anti-sheep erythrocyte antibody production was obtained at a dose of 25 IU of L-asparaginase/mouse, whereas 1000 IU in either single or divided doses failed to cause inhibition after rechallenge with sheep erythrocytes. Allogeneic tumor take was observed when mice were treated with more than 200 IU of L-asparaginase, but no tumor take occurred in mice preimmunized with the same tumor. The immunosuppressive action of L-asparaginase appears to affect not only the production of circulating antibody but also the cellular immunological reactivity.

- 1561 IMMUNOLOGICAL ENHANCEMENT OF MURINE TUMOR ISOGRAFTS MEDIATED BY RNA FROM LYMPHOID ORGANS OF XENOGENIC IMMUNIZED ANIMALS. (E.) Pilch, Y. H. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and K. P. Ramming. *Transplantation* 11(1):10-19, 1971.

RNA prepared from spleen and lymph node tissue of guinea pigs immunized with cell suspensions derived from a benzpyrene-induced sarcoma was incubated with normal mouse spleen cells and cells from the same sarcoma; this mixture was inoculated into C3H mice, and resulted in enhanced sarcoma growth. Ninety-two percent of mice given immune RNA-normal spleen and sarcoma cells developed sarcomas, the first tumor appearing 8 days after inoculation; 36% of control mice given tumor cells only developed tumors, the first of which appeared on day 25. When mice were given sarcoma cell isografts mixed with spleen cells treated with RNA from guinea pigs immunized with normal mouse tissue, tumor growth was also enhanced; however, there was a longer latency period (15 days) compared to inoculation with spleen cells incubated with RNA from immunized guinea pigs. RNA from guinea pigs immunized with Freund's adjuvant also produced tumor enhancement. Enhancement of tumor growth was specific for the immunizing tumor, since RNA from guinea pigs immunized with cells from 1 line of benzpyrene-induced tumor produced enhancement of growth for that tumor, but not for a related benzpyrene-induced tumor. Serum from mice in which enhancement of tumor growth had been produced by RNA from immunized guinea pigs markedly facilitated the growth of tumor cells incubated with this serum, suggesting the presence of an enhancing antibody in serum of mice in which enhanced growth of tumors had been produced by RNA-incubated spleen cells. No enhancement of tumor growth was produced when mice were given mixtures of tumor cells and spleen cells preincubated with RNA from guinea pigs immunized with RNase-treated benzpyrene-induced sarcoma cells. In 3 out of 5 experiments, no tumor growth enhancement was observed in mice inoculated with sarcoma cells and untreated spleen cells.

- 1562 A GROWTH-MODIFYING FACTOR FROM CELL LINES OF HUMAN MALIGNANT ORIGIN. (E.) Rounds, D. E. (Pasadena Found. Med. Res., Calif.). *Cancer Res* 30(12):2847-2851, 1970.

An attempt was made to isolate and characterize a factor which has a measurable effect on the growth and morphology of fibroblasts derived from human carcinoma cells and human embryonic skin. Cell-free culture media harvested from flasks of KB (nasopharyngeal), CMP (colon), and HeLa (cervical) cells were found to be toxic to fibroblasts derived from human embryonic skin with KB and CMP showing qualitatively greater toxicity after 48 hr. The media contained a prealbumin band in an acrylamide gel electrophoretic core, which was absent in aliquots of media that had not been used to sustain cell growth. No such band could be detected from media that had supported growth of human embryonic skin fibroblasts. Anti-

growth modifying factor (GMF) serum reacted with antigens from culture medium which had supported the established lines of KB, CMP, HeLa and amnion cells. Precipitin lines were continuous in antigens of the first three mentioned. No antigens that would react with anti-GMF serum were found from either control or nutrient fluid harvested from fibroblast cultures. Anti-human prealbumin showed a positive reaction with electrophoretically separated human serum prealbumin, but was not reactive at the same concentration with antigen derived from 48-hr cultures of CMP cells. Synthetic products from the 3 malignant cell lines were nondialyzable, showed positive reactions for peptides and proteins, were insoluble in alcohol and trichloroacetic acid and showed absorption maximum at 280 nm. Mitotic activity of fibroblasts could be stimulated and an increase in total cell number was noted with a concentration of 0.2 g/ml of CMP protein but increasing concentrations completely abolished this activity, and cell population was reduced by nearly 15%. That fibroblasts can be either stimulated or inhibited by varying concentrations of GMF could account for conflicting reports of the effects of tumor extracts on connective tissue elements.

- 1563 THE PURIFICATION AND PARTIAL CHARACTERIZATION OF A SERUM FACTOR ASSOCIATED WITH A NEOPLASM IN GOLDEN HAMSTERS. (E.) Hawthorne, C. (Dept. Zool., U. Vermont, Burlington), V. Riggs, D. F. Stevens and D. L. Weller. *Biochem Biophys Res Commun* 42(2):166-172, 1971.

A serum factor which promotes or induces cleavage in multinucleated cells in the presence of estrogen was purified from fractions of ascites fluid from ascites tumors of hamsters. The method employed permitted 5000-fold purification of the factor. Electrophoretic analysis of the fractions of hamster ascites tumors showed that the prealbumin band increased in concentration until only this band was visible in the electrophoretogram; the band showed cytokinetic activity when extracted from the acrylamide gel; sera from normal hamsters, while concentrating in the prealbumin band, did not show cytokinetic activity. The ascites serum factor concentrated on electrofocusing in the region of pH 5.5-5.8. It was suggested that the factor was a polypeptide or protein.

- 1564 γ A HALF MOLECULES: DEFECTIVE HEAVY CHAIN MUTANTS IN MOUSE MYELOMA PROTEINS. (E.) Mushinski, J. F. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *J Immunol* 106(1):41-50, 1971.

Two different types of γ A myeloma proteins were compared using the secretory products of two closely related tumors isolated from a single primary tumor-bearing BALB/c mouse. Ultracentrifugal analyses of the 2 γ A myeloma proteins isolated from serum showed sawtooth heterogeneity, and both exhibited different degrees of polymer formation which progressed spontaneously in solution. The mean molecular wt of 68,000 was consistent with the presence of one light chain of around 23,000 bound to a heavy chain of around 45,000 molecular wt. Completely reduced and

alkylated heavy chains of the 2 proteins were soluble in concentrated urea and guanidine HCl, and urea-Sephadex G-100 determinations yielded an average molecular wt of about 46,000 for one heavy chain (a polymeric molecule) and about 54,000 for the other (a 2-chain molecule), indicating a statistically significant difference ($p=0.0169$). Preliminary amino acid analysis showed that 5 tryptic peptides accounted for no more than 24 of the expected 80 or so amino acid residue difference between the polymeric-type heavy chain and the 2-chain forms. Direct chemical localization of the polypeptide segment present in the polymeric heavy chain and not in the 2-chain protein is being attempted.

- 1565 BIOSYNTHESIS OF THE CARBOHYDRATE PORTION OF IMMUNOGLOBULIN: RADIOCHEMICAL AND CHEMICAL ANALYSIS OF THE CARBOHYDRATE MOETIES OF TWO MYELOMA PROTEINS PURIFIED FROM DIFFERENT SUBCELLULAR FRACTIONS OF PLASMA CELLS. (E.) Melchers, F. (Max Planck Inst. Molec. Genet., Berlin, Germany). *Biochemistry* 10(4):653-659, 1971.

Myeloma proteins from the subcellular fractions of 2 mouse plasma cell tumors were assayed. Cell homogenates from the tumors (called MOPC21 and MOPC46) were fractionated by density gradient centrifugation. Centrifugation yielded 3 subcellular fractions: smooth membrane (without ribosomes), rough membrane (with ribosomes), and cytoplasmic supernatant. Myeloma protein was detected in all 3 fractions. The cytoplasmic fraction contained between 3-30% of the total intracellular myeloma protein, indicating that at least 97% of protein may be compartmentalized in membranous structures in the plasma cells. This suggested that the protein in the cytoplasmic supernatant fraction represented an artifact in the preparation of cell homogenates. The 2 types of plasma cell tumor had similar distributions of myeloma protein among their subcellular fractions; they showed similar kinetics of tritiated leucine and tritiated monosaccharide incorporation into their myeloma proteins. The subcellular distribution of ^3H -mannose, ^3H -glucosamine and ^3H -galactose in the tumors was investigated by labeling cells for 6 hr with the radioactive proteins. Myeloma protein associated with rough membrane contained glucosamine and mannose residues, but only traces of galactose and no fucose; smooth membrane myeloma proteins contained residues of glucosamine, mannose and galactose and traces of fucose. The relative amounts of mannose, galactose, glucosamine and fucose located in the 3 subcellular fractions was virtually identical in the 2 types of plasma cell tumor. The results appeared to support the hypothesis that addition of carbohydrate residues to immunoglobulins proceeds in several stages and in different areas of the plasma cells.

- 1566 FETAL GUT ANTIGEN: A SUBSTANCE IN FETAL GUT AND ITS RELATIONSHIP TO GUT CARCINOMA. (E.) Smith, J. B. (Natl. Naval Med. Ctr., Bethesda, Md.) and R. T. O'Neill. *Res Commun Chem Path Pharmacol* 2(1):1-15, 1971.

The presence in human fetal gut of an antigen, fetal gut antigen or FGA, was determined in micro double-

diffusion tests using antiserum prepared by injecting a rabbit with human fetal gut extracts. FGA was found to have an electrophoretic mobility similar to that of beta-globulins; it was found in 87% of gut extracts from human fetuses aged 10-34 wk. FGA was also found in the liver of 2 fetuses, in the lung of another and in the skin of a fourth. FGA was found in 8% of tissues from the gastrointestinal system of normal humans and in 31% of tissues from human gastrointestinal systems affected with malignancies or ulcerative colitis. FGA was not found in malignant tissues other than the gastrointestinal tract, except in tissue from a Wilm's tumor. FGA was found in 1 of 452 human serum samples studied; the serum was prepared from a patient with gastrointestinal metastases from a laryngeal carcinoma. The antigen was not found in normal fetal serum, in the serum of pregnant women, nor in the serum of patients with gastrointestinal tract malignancies.

- 1567 AN IMMUNOLOGICAL STUDY OF SOME HUMAN BRAIN TUMORS CONCERNING THE BRAIN SPECIFIC PROTEIN S_{100} . (E.) Haglid, K. G. (Inst. Neurobiol., U. Gothenburg, Sweden) and C. A. Carlsson. *Neurochirurgia* 14(1):24-27, 1971.

A method for differentiating between primary and secondary brain tumors and for indicating the origin of brain tumors has been analyzed utilizing specific protein S_{100} . Normal brain tissue and tumors originating from glial cells showed a positive reaction to anti S_{100} ; undiluted homogenates of normal brain had the most positive reaction with antiserum dilutions of 1:5 and 1:10. Those tumors showing positive reactions included astrocytomas, spongioblastomas, glioblastoma multiformes and gliomas of supratentorial, infratentorial and spinal cord origin, while negative findings were reported from ependymomas, meningiomas, adenomas, sarcomas and metastatic lesions of supratentorial and infratentorial origin. Using an immunological technique, a protein antigenically identical with the S_{100} protein was found to be present in tumors of glial origin but was missing in tumors originating from non-glial structures.

- 1568 A NEW MOUSE IMMUNOGLOBULIN: IgG3. (E.) Grey, H. M. (Natl. Jewish Hosp. Res. Ctr., Denver, Colo.), J. W. Hirst and M. Cohn. *J Exp Med* 133(2):289-304, 1971.

The structural and biologic properties of a new mouse immunoglobulin, IgG3, were studied in the J606 murine myeloma tumors by immunodiffusion, immunoelectrophoresis and radial immunodiffusion methods. The J606 protein was first identified as an immunoglobulin showing a reaction on an Ouchterlony diffusion slide with a beta 2-6-linked levan showing 1 major band on acrylamide gel electrophoresis, which showed as 2 or 3 closely running bands of decreasing intensity upon dilution. Papain digested the protein into 2 fragments which were non-crossreacting, and a single homogeneous peak was eventually obtained with a sedimentation coefficient of 5.85 upon ultracentrifugation. The intact protein had a molecular wt of 150,000, and the slow-migrating papain fragment had

a molecular wt of 47,000. After partial reduction and alkylation of J606 protein, heavy and light chains with molecular wt of 50,000 and 23,000, respectively, were separated; the heavy chain possessed 9-10 carboxymethyl cysteines after complete reduction and alkylation. Relatively high concentrations of the protein were noted in newborn mice, probably due to placental transport. This new protein was shown to be present in normal mouse serum at a concentration of 0.1-0.2 mg/ml.

- 1569 SERUM GROUP-SPECIFIC (Gc) PROTEIN CONCENTRATIONS IN PATIENTS WITH CARCINOMA, MELANOMA, SARCOMA, AND CANCERS OF HEMATOPOIETIC TISSUES AS DETERMINED BY RADIAL IMMUNODIFFUSION. (E.) Hughes, N. R. (Prince of Wales Hosp., Randwick, New South Wales, Australia). *J Nat Cancer Inst* 46(3):665-675, 1971.

An examination of sera from 1,238 samples taken from patients with cancer of 29 sites, and from 256 normal controls indicated that the mean concentrations of group-specific (Gc) protein in serum was higher in females than it was in males in both the cancer group and in controls. Female patients with malignant melanoma also showed higher mean Gc protein concentrations than males with malignant melanoma. Females with breast cancer or carcinoma of the colon and rectum also had higher Gc protein concentrations than normal males and males with carcinoma of the colon and rectum, resp. The mean concentration of Gc protein in sera from all cancer patients combined did not differ significantly from that of controls. Males with lymphatic tumors other than lymphatic leukemia, fibrosarcoma, osteogenic sarcoma, poorly differentiated sarcoma, or Ewing's tumor had higher concentrations of Gc protein than did normal males. For both controls and cancer patients, significant differences in mean Gc protein concentration were found between sera of different Gc groups; the highest Gc protein levels were found in group Gc 1:1 sera and the lowest in group Gc 2:2 sera.

- 1570 IMPAIRED *IN VITRO* RESPONSE OF CIRCULATING LYMPHOCYTES TO PHYTOHEMAGGLUTININ IN DOWN'S SYNDROME: DOSE- AND TIME-RESPONSE CURVES AND RELATION TO CELLULAR IMMUNITY. (E.) Rigas, D. A. (U. Oregon Med. Sch., Portland), P. Elsasser and F. Hecht. *Int Arch Allerg* 39(5-6):587-608, 1970.

Lymphocytes from venous blood of 9 patients with Down's syndrome and 9 healthy subjects were treated with phytohemagglutinin (PHA) in varying doses; it was found that the incorporation *in vitro* of ^{14}C -labeled thymidine into the DNA of the lymphocytes stimulated with PHA was significantly impaired in Down's syndrome patients as compared to normals. At doses of 0.001 mg of PHA/ml of culture, the incorporation of thymidine in Down's syndrome patients was consistently impaired; at this dose, the amount of thymidine incorporated by lymphocytes of patients with Down's syndrome was about 70% that of normal subjects. A minimal response of thymidine incorporation which occurred at a dose level of 0.0005 mg PHA/ml and in the absence of PHA was consistently higher in Down's syndrome patients than in normal subjects.

Dose-response studies showed that the optimal dose of PHA for maximum thymidine incorporation by lymphocytes was 0.005 mg/ml culture, which caused more than 3 times as much thymidine incorporation in normal subjects as in Down's syndrome patients. The immune deficiency suggested by the impaired lymphocyte response to PHA in Down's syndrome may be related to the high incidence of leukemia seen in patients with this condition.

1571 A ROLE FOR RED CELLS IN PHYTOHEMAGGLUTININ-INDUCED LYMPHOCYTE STIMULATION. (E.)

Tarnvik, A. (Dept. Clin. Bacteriol., U. Umea, Sweden). *Acta Path Microbiol Scand* 78(6):733-740, 1970.

The influence of various blood cell types on phytohemagglutinin (PHA)-induced lymphocyte stimulation was investigated using venous blood from healthy donors. The PHA-response of lymphocytes was measured by the *in vitro* incorporation of ^3H -thymidine by the lymphocytes. Lymphocytes prepared in cultures with the buffy coat of whole blood incorporated 85.7×10^3 cpm of ^3H -thymidine, while purified lymphocytes incorporated 37.3×10^3 cpm ^3H -thymidine; purified lymphocytes with added filtered blood cells (4×10^6 RBC/ml) incorporated 91.2×10^3 cpm radioactive label. When purified lymphocytes were incubated in the presence of varying numbers of RBC, the thymidine incorporation by the lymphocytes was dependent on the number of RBC added to the incubation mixture. Incubation of lymphocytes with mitomycin-treated monocytes and platelets also increased the incorporation of ^3H -thymidine by PHA-stimulated lymphocytes over that observed for purified stimulated lymphocytes alone.

1572 STUDIES OF THE AFFINITY OF NUCLEAR MATERIAL FOR UROPORPHYRIN: II. PHYTOHEMAGGLUTININ "TRANSFORMED" RAT PERITONEAL LYMPHOCYTES. (E.)

Hartmann, G. R. (Dept. Med., U. Minnesota, Minneapolis) and C. J. Watson. *Biochem Med* 4(5-6):403-407, 1970.

The effect of uroporphyrin on Sprague-Dawley rat mononuclear cells stimulated *in vivo* by phytohemagglutinin was studied by fluorescence microscopy. After 10 days of daily i.p. administration of phytohemagglutinin-P the rat peritoneal fluid contained many cells of the relatively large, immature or "blastic" type referred to as "transformed" lymphocytes which exhibited an affinity for uroporphyrin revealed by a distinct red nuclear fluorescence which persisted after repeated washings with normal saline or fetal calf serum. Cells aspirated prior to uroporphyrin injection exhibited no red fluorescence. Similarly, untreated rats injected with uroporphyrin failed to exhibit cellular red fluorescence. Nuclear fluorescence of the transformed cells did not increase upon addition of 0.1 N HCl, a phenomenon which is generally observed with Ehrlich ascites tumor cells even though the affinity of nuclear material for uroporphyrin paralleled the behavior of the tumor cells.

1573 EVIDENCE FOR THYMIC DEPENDENCE OF PHA-REACTIVE CELLS IN SPLEEN AND LYMPH NODES AND INDEPENDENCE IN BONE MARROW. (E.) Blomgren, H.

(Karolinska Inst., Stockholm, Sweden) and E. Svedmyr. *J Immun* 106(3):835-841, 1971.

The role of the thymus was studied during recovery of the phytohemagglutinin (PHA) response in the spleen, lymph node and bone marrow cells of mice of strains CBA and BALB/c which were lethally X-irradiated and protected with bone marrow and fetal liver cells. *In vitro* PHA response was lowest 8-10 days after irradiation in the thymus, spleen and lymph node cells and increased to values found in non-irradiated controls at 35-55 days; these values remained low in controls containing no PHA in the cultures. In contrast, the response of the bone marrow cells was high at 8 days and remained constant during the period of observation. Mice that were thymectomized 3-4 wk before irradiation showed lower reactivity in spleen and lymph node cells compared to thymectomized mice treated additionally with thymic cells or to mice undergoing sham thymectomy; bone marrow cells from all 3 groups were more or less equal. The differences in the PHA response paralleled the differences in the number of nucleated cells; comparable differences were observed when the mice were injected with fetal liver cells. Pretreatment of lymph node cells from both strains of mice with antiserum drastically reduced the response of the surviving cells, but this effect was not seen with bone marrow cells. These results indicate that the responsive cells in the bone marrow are not thymus-derived, and theta-bearing cells in the lymph nodes are mainly responsive to phytohemagglutinin. In the bone marrow a theta-negative cell population can also be activated by PHA.

1574 *IN VITRO* RESPONSES OF LYMPHOCYTES FROM CANCER-BEARING PATIENTS TO AUTOCHTHONOUS TUMOR TISSUES. (E.) Hsu, C. C. S. (Mt. Sinai Hosp., New York, N. Y.) and S. R. Cooperband. *Proc Soc Exp Biol Med* 136(2):446-448, 1971.

Tumor and normal tissues from 10 patients who underwent surgery for malignancy were incubated with blood lymphocytes from the same patient donors in order to investigate lymphocyte proliferation as a response to autochthonous tumor cells. The tumors were carcinomas from the stomach, breast and rectum. Four of 6 patients were positive when tested for the presence of intact delayed hypersensitivity. Lymphocytes from all patients showed a proliferative response to phytohemagglutinin, with large numbers of cells showing blast transformation. Incorporation of tritiated thymidine by DNA of the phytohemagglutinin-stimulated cells was relatively low. The lymphocyte responses of the patients to autochthonous tumor tissue and normal tissue were not markedly different, and no general lymphocyte response to the tumor cells could be demonstrated.

1575 STUDIES ON MALIGNANT TUMOR AND ANEMIA. X. IMMUNOLOGICAL INVESTIGATION ON MUCO-PROTEIN IN CANCEROUS URINE AND ANAEMIA-INDUCING SUBSTANCE IN HUMAN PLACENTA. (Jap.) Ogata, K. (Fac. Med. Hirosaki U., Japan). *Hirosaki Med J* 22(2):251-263, 1970.

The Ouchterlony method was employed to determine whether the mucoprotein from urine of cancer patients and the human placental anemia-inducing substance P-62 have a common antigen. Urine specimens were prepared from patients with and without malignancy and antiserum against the placental anemia-inducing substance was prepared by immunizing rabbits with complete Freund adjuvant. A characteristic precipitation was seen on gel diffusion between a fraction from cancer patients' urine and the anti-P-62 antiserum, while the same fraction from normal urine showed no reaction with anti-P-62. The locus of the precipitation was at the position corresponding to the γ M and/or the γ A-globulin regions. Apparently, the mucoprotein in urine of cancer patients does have antigen in common with the anemia-inducing substance in human placenta.

- 1576 IMMUNE FUNCTION IN MULTIPLE MYELOMA: IMPAIRED RESPONSIVENESS TO KEYHOLE LIMPET HEMOCYANIN. (E) Harris, J. (U. Texas M.D. Anderson Hosp. & Tumor Inst., Houston), R. Alexanian, E. Hersh and P. Migliore. *Canad Med Ass J* 104(5):389-393, 1971.

An investigation into the immune deficiency state associated with multiple myeloma in man was made by immunization with keyhole limpet hemocyanin (KLH) of 23 patients with multiple myeloma, 4 patients with treated localized plasmacytoma and 14 normal subjects and by evaluation of antibody formation and hypersensitivity response as well as *in vitro* lymphocyte blastogenesis. By the 7th postimmunization day, control subjects developed antibody to KLH but only 8 out of 23 of the myeloma patients showed detectable antibody which reached a peak median titer for total antibody of 4 (dilution 1-16), compared to a value of 6 (dilution 1-64) for the normal subjects. Decline in titer was noted after 14 days in the myeloma group, but the control group titers plateaued until at least 56 days after immunization. Immune responses of the plasmacytoma group were in the normal subject range. All normal subjects had developed delayed hypersensitivity to the agent by day 7 while 8 of 10 myeloma patients gave positive reactions with 2 additional subjects showing positive results on day 14. Both control and myeloma patients showed a slight but definite response *in vitro* to the agent prior to immunization with the myeloma group showing impaired response over a period of 14 days (the median response for the myeloma group was 2700 cpm compared to 6800 cpm for the controls which tended to plateau thereafter). Immunologically competent lymphocytes of both "thymus-dependent" and "immunoglobulin-producing" types are abnormal in patients with clinically overt multiple myeloma.

- 1577 COMPARATIVE STUDIES OF ANTIGENS PRESENT IN NEUROBLASTOMAS AND IN FETAL AND ADULT ADRENALS. (Fr.) Kohen, M. (Inst. Res. Sci. Cancer, Villejuif, France), D. Buffe and P. Burtin. *Bull Cancer* 57(3):355-364, 1970.

Five tissue antigens were found in soluble extracts from neuroblastomas and from human adult and fetal adrenals in an immunochemical study. None of the antigens was found to be specific for the neuroblastoma, and none were found to be specific for normal adult or fetal adrenal tissue. On electrophoretic precipitation, all the different precipitin lines produced by the antigens appeared as proteins; no evidence of lipids, glycoproteins or nucleic acids were found. Esterase activity was demonstrated for 2 of the 5 antigens. In fetal adrenals, α_1 -fetoprotein was present, but in sera from children with neuroblastomas, neither tumor specific antigen nor anti-tumor antibodies could be detected. Positive reactions were seen between some patients' sera and some antineuroblastoma antisera, but these reactions were thought to be due to a nonspecific tumor antigen, α_2 H-globulin, which was found in the sera of many of the cancer patients.

- 1578 CONCURRENT INFECTIOUS MONONUCLEOSIS AND ACUTE LEUKEMIA: CASE REPORTS, REVIEW OF LITERATURE AND SEROLOGIC STUDIES WITH THE HERPES-TYMPUS VIRUS (EB VIRUS). (E.) Stevens, D. A. (Stanford U. Hosp., Palo Alto, Calif.), P. H. Levine, S. K. Lee, M. J. Sonley and D. E. Waggoner. *Amer J Med* 50(2):208-217, 1971.

High titers of Epstein-Barr virus (EBV) antibodies were found in 2 cases of infectious mononucleosis (IM) which developed following the diagnosis of acute lymphocytic leukemia (ALL). In these 2 new cases, and in 5 previously recorded cases of concurrent IM and ALL, the elapsed time from ALL onset to IM onset was 2-45 months; in the 2 new cases, the development of IM in the course of ALL appeared to have a favorable effect on ALL. In 1 case EBV antibody titers rose from 40 prior to onset of IM to 160-2,560 following IM; and in the second new case antibody titers rose from 160 to 2,560 in 6 months following the onset of IM. Geometric mean titers anti-EBV antibody for late-stage ALL patients, pretherapy ALL patients, patients with hematologic diseases, and patients without malignant disease were similar (titers of 1:12-1:32); however, anti-EBV antibody titers for long-term ALL survivors were consistently higher than titers in the former groups (geometric mean titers of 1:161). These differences were significant only in the comparison of long-term ALL survivors with non-malignant patients and late stage ALL patients. No correlation could be shown between high anti-EBV titer and length of survival of ALL patients. In the 2 new cases of concurrent IM and ALL, a secondary rise in EBV antibody titer was seen after recovery from IM; in IM patients without ALL, EBV antibody titers fell after recovery from IM, indicating that the sustained rise in EBV antibody titer in the IM-ALL cases is due to the concurrence of the 2 diseases.

- 1579 LYMPHOCYTE INFILTRATION IN BLADDER CARCINOMA. (E.) Tanaka, T. (Sch. Med. U. Leeds, England), E. H. Cooper and C. K. Anderson. *Rev Eur Etud Clin Biol* 15(10):1084-1089, 1970.

Urinary bladder tumors were examined to investigate the extent of lymphocyte infiltration and to correlate lymphocyte infiltration with the pathological type of lesion and with the clinical course. The case material consisted of 1,090 specimens of bladder tumor from 762 English patients. Twenty-four percent of the tumors were benign lesions, including epithelial hyperplasia, cystitis cystica or glandularis, fibrosis or leukoplakia; 73% were carcinomas, 32% of which were well-differentiated, 22% were poorly-differentiated, and 18% were anaplastic. The remainder of the examined specimens included carcinoma *in situ* and carcinoma invasion from the uterus or rectum into the urinary bladder. Lymphocytic infiltration was more often seen in carcinomas than in benign lesions; diffuse lymphocytes were found in 6 benign lesions, in 40 well- and poorly-differentiated carcinomas, and in 28 anaplastic carcinomas. Survival of patients was similar in cases showing lymphocytic infiltration and in patients without infiltration. The reasons for the variations among tumors in the presence of and in the degree of lymphocyte infiltration are obscure; tumors showing marked lymphocytic infiltration may be more antigenic than other tumors.

- 1580 THE DEMONSTRATION OF α -FETOPROTEIN IN HUMAN TUMOR ASCITES AND ITS PARTIAL PURIFICATION. (Ger.) Rapp, W. (Med. U. Clin. Heidelberg, Germany) and H. E. Lehmann. *Clin Chim Acta* 31(1): 43-53, 1971.

- 1581 THE PRIMARY STRUCTURE OF A MONOCLONAL γ 1-IMMUNOGLOBULIN (MYELOMA PROTEIN NIE): I. AMINO ACID SEQUENCE OF THE VARIABLE PART OF THE H-CHAIN, SUBGROUPS OF VARIOUS REGIONS. (Ger.) Ponsstingl, H. (Max Planck Inst. Exp. Med., Gottingen, Germany), J. Schwarz, W. Reichel and N. Hilschmann. *Hoppe Seyler Z Physiol Chem* 351(12):1591-1594, 1970.

- 1582 PRIMARY CARCINOMA OF THE CERVIX APPEARING IN IMMUNOSUPPRESSED RENAL TRANSPLANT RECIPIENT. (E.) Tallent, M. B. (Dept. Surg., U. Minnesota, Minneapolis), R. L. Simmons and J. S. Najarian. *Amer J Obstet Gynec* 109(4):663-664, 1971.

- 1583 LENTINAN, A NEW IMMUNO-ACCELERATOR OF CELL-MEDIATED RESPONSES. (E.) Maeda, Y. Y. (Nat'l. Cancer Ctr. Res. Inst., Tokyo, Japan) and G. Chihara, *Nature* 229(5287):634, 1971.

See also:

- * (Chem): 1324, 1325
- * (Viral): 1448, 1449, 1451, 1467, 1468, 1476, 1477, 1495, 1510
- * (Path): 1587

- 1584 *IN VITRO* "SPONTANEOUS" NEOPLASTIC TRANSFORMATION OF MOUSE FIBROBLASTS IN DIFFUSION CHAMBERS. (E.) Parmiani, G. (Nat'l. Tumor Inst., Milan, Italy), G. Carbone and R. T. Prehn. *J Nat Cancer Inst* 46(2):261-268, 1971.

Muscle cells of newborn mice were placed in diffusion chambers 13 mm in diameter containing millipore filters with outside and inner porosities of 0.45 and 1.2 μ , resp. Loaded diffusion chambers were placed in a liquid culture medium or in the peritoneal cavity of syngeneic mice; at 4 wk intervals from the 8th to the 36th wk of culture, diffusion chambers were opened and the growth of the enclosed tissue was observed. At these times, fragments of muscle tissue were implanted s.c. into immunodepressed mice to test the tissue for oncogenicity. It was found that 44 of 52 diffusion chambers maintained *in vivo* within mice contained growing cells, while only 15 of 44 diffusion chambers maintained *in vitro* contained growing cells. No neoplastic transformation was evident in cells cultured in diffusion chambers maintained *in vivo*; none of the 44 mice given transplants of the tissue developed tumors for 50 wk after transplantation. However, 5 of 15 diffusion chambers maintained *in vitro* gave rise to tumors when transplanted in mice; after 20 wk *in vitro*, surviving cells from all diffusion chambers produced tumors. Tumors obtained from *in vitro* transformed tissue did not show significant antigenicity. Apparently neoplastic transformation of the cells in the diffusion chambers depended on the field medium provided by *in vitro* cultivation.

- 1585 FINE STRUCTURE OF RESERVE CELL HYPERPLASIA AND INCOMPLETE SQUAMOUS METAPLASIA OF THE UTERINE CERVIX. (E.) Laguens, R. P. (Sci. Invest. Comm. Prov. Buenos Aires, La Plata, Argentina), J. Lagrutta and F. Quijano. *Int J Gynaec Obstet* 9(2): 41-49, 1971.

Cervical biopsy specimens taken from nonpregnant patients aged 19-42 yr with reserve cell hyperplasia and incomplete squamous metaplasia of the uterine cervix were examined by electron microscopy. Columnar mucus cells of reserve cell hyperplasia patients were similar to those in normal endocervical epithelium; they had numerous microvilli, abundant cytoplasmic secretion droplets, and meager cytoplasm. Nucleoli of these cells were unusually large. Microvilli of cells touched those of nearby cells and defined irregular intercellular spaces. Mitochondria, endoplasmic reticulum and Golgi apparatus were not well developed. Cells in biopsies from patients with incomplete squamous metaplasia showed a marked polymorphism, with 3 cell types being prominent. One cell type appeared as small cells with scarce cytoplasm of high electron density, and was similar to the hyperplastic reserve cell type. The second cell type was represented by typical columnar mucus cells, and the third type appeared as large cells with abundant cytoplasm and a well-developed rough endoplasmic reticulum; these cells resembled normal endo- and exocervical cells. The hyperplastic reserve cells may be the origin of severe cervical dysplasia and carcinoma *in situ*, and their prolifer-

ation and incomplete differentiation may result in incomplete squamous metaplasia.

- 1586 MORPHOGENESIS OF EXPERIMENTAL KIDNEY TUMORS IN HAMSTERS. (Rus.) Yermolova, T. S. (Inst. Orenburg, U.S.S.R.) and L. A. Cherkasskiy. *Onkol* 16(11):55-61, 1970.

The morphogenesis of synestrol-induced kidney tumors in hamsters was investigated. Four experimental groups were used: 1) 33 male hamsters were given 2 mg synestrol s.c. once a month for 14 months; 2) 16 male hamsters were given 20 mg synestrol s.c. for 10 months; 3) 19 female hamsters received 2 mg synestrol s.c. for 11 months and 4) 25 female hamsters were subjected to ovariectomy prior to the 2 mg synestrol s.c. treatment for 8 months. Of the alterations first noticed in the kidney tissue following synestrol administration (dysproteinosis, granular dystrophy, amyloidosis), the proliferation of straight and convoluted tubular epithelial cells was most closely related to the later development of tumors. Epithelial cell proliferation was noticed in all male hamsters on the 17-20th day and in the female hamsters of group 3 and 4 on the 68th day after the beginning of the experiment. The female hamsters developed tumors. The progressive development of convoluted tubular epithelium in male hamsters led to the formation of adenomas, beginning on the 312th day in the animals of the group 1 and on the 220th day in the hamsters of the group 2. Multiple bilateral tumors appeared in 6 males of the group 1 and in 3 males of group 2 on the 321-418th day and 267-311th day, respectively. The weight of the tumor-invaded kidney varied from 400 to 5650 mg. Three hamsters showed metastasis to the spleen and diaphragm. The tumor nodules were not encapsulated and had rather diffuse boundaries. The presence of small adenomas and dispersed groups of proliferated intertubular histiocytes was also noticed.

- 1587 ONTOGENESIS AND PRECANCEROUS CHANGES OF SERUM GLOBULINS IN MICE: ESPECIALLY IN RELATION TO PATHO-MICROSCOPIC FINDINGS IN VARIOUS ORGANS. (E.) Yokota, Y. (Fac. Med. Shinshu U., Japan). *Med J Shinshu Univ* 15(1):17-46, 1970.

Serum changes occurring in normal mice of various strains following birth and in mice sensitized with a plasma-cell producing tumor antigen were investigated. The ultracentrifugation pattern of the serum of normal newborn mice showed 2 peaks of 6S and 7S. Reticulum cells were predominant in the bone marrow of normal mice, and no plasma cells could be seen. The total serum protein decreased after antigen sensitization; between 4-48 wk after sensitization, protein concentrations in the different mouse strains dropped in many cases to half their 4 wk values. Concentrations at 40-48 wk clustered around 4% for different strains. In BALB/c and C3H strain mice, 4S, 7S and 18-20S peaks were present in the serum from 8-26 wk after sensitization; after 26 wk, only 4S and 18-20S peaks were present. In sensitized mice, plasma cell infiltration was localized chiefly around the arteriolar region; infiltration increased with time after sensitization but became negligible after 26 wk postinjection.

1588 DIFFERENTIATION OF MALIGNANT TO BENIGN CELLS. (E.) Pierce, G. B. (U. Colorado Med. Ctr., Denver) and C. Wallace. *Cancer Res* 31(2): 127-134, 1971.

Rats bearing well-differentiated squamous cell carcinomas of the lip were given injections of ³H-thymidine for the purpose of observing the proportion of labeled nuclei in undifferentiated and well-differentiated tumor cells. Tumors consisted of well-differentiated tissue, with squamous pearls separated from one another by undifferentiated cancer cells. Two hr after ³H-thymidine was injected, most of the label was incorporated into the undifferentiated cancer cells, and only 5 labeled cells were found in the well-differentiated squamous pearls. By 50 hr post-injection, the number of labeled cells in the undifferentiated cells had declined markedly, and there were 56 ³H-labeled cells in the pearls. By 96 hr postinjection, the number of labeled cells in the pearls had increased to 219. Tumor growth apparently dependent on proliferation of undifferentiated cells and the growth of the pearls depended on assimilation of the undifferentiated cells into the pearl. Electron microscopy showed that undifferentiated cells which were incorporated into pearls became well-differentiated. Undifferentiated and well-differentiated cells were transplanted into compatible hosts with the result that of 82 undifferentiated cells transplanted, 27 developed into tumors in 7 months; of 78 well-differentiated pearl-cell transplants, none developed into tumors.

1589 PATHOGENESIS OF LYMPHORETICULAR NEOPLASMS IN TRANSPLANT RECIPIENTS. (Ger.) Krüger, G. (Natl. Cancer Inst., Natl. Inst. Hlth, Bethesda, Md.). *Verhandl Deutsch Ges Path* 54:175-181, 1970.

Reports of tumors in lymphoreticular tissue after organ transplantation and the associated immunosuppressive treatment led to these experiments to determine if simultaneous chronic antigen stimulation and immunosuppression can effect lymphomagenesis. Mice were subjected to immunosuppression by thymectomy, splenectomy, Imuran with and without antilymphocytic serum or Dilantin, and antigenic stimulation with LDH virus, vaccinia virus, tumor cells, complete adjuvant, HeLa cells or Dilantin. Of these combinations, only 2 (the Dilantin-Dilantin and the Imuran-antigen) showed lymphomagenesis, while the others revealed an increased proliferation of normal cells with neoplastic characteristics in some cases. The controls with only continuous antigen stimulation or with only immunosuppressive treatment led to regressive proliferative changes, but not to tumors. In the transplantation of foreign tissue the continuous antigen stimulation of the recipient and the need to suppress antibody formation result in the formation of lymphoreticular neoplasm.

1590 ARGYROPHIL CELL: HYPERPLASTIC, PRE-NEOPLASTIC AND NEOPLASTIC PROLIFERATIONS: A PRELIMINARY OBSERVATION. (E.) Soga, J. (Niigata U. Sch. Med., Japan) and T. Hatano. *Acta Med Biol Niigata* 18(1):1-6, 1970.

Behavior of argyrophil cells in human gastric and colonic carcinomatous mucosa was studied in 36 individuals by means of argentaffin reactions. In 8

of 20 cases with gastric carcinoma and 3 of 16 cases with colonic carcinoma, increased numbers of argyrophil cells close to the malignant lesions were seen primarily in the base of the glands. In the *Mastomys* gastric mucosa, argyrophil cells were observed in scattered foci of 2 or 3 cells near argyrophil cell neoplasia and appeared to be hyperplastic proliferation possibly of a reactive nature. Furthermore, normal portions of the glandular stomach bearing argyrophil neoplasms showed lesions differing from the above-mentioned; the gastric gland configuration was preserved but was completely replaced by the argyrophil cells and hence have been classified as "pre-neoplastic or pre-invasive". Further serial sections of the same portions of the stomach indicated the formation of a microneoplasm. It is postulated that the argyrophil cells in pre-neoplastic proliferation in the mucosa of *Mastomys* glandular stomach may subsequently develop into neoplastic and invasive stages followed by typical polypoid tumor formation.

1591 JUVENILE POLYPS OF THE COLON. (E.) Holgersen, L. O. (St. Luke's Hosp. Ctr., New York, N. Y.), R. E. Miller and H. A. Zintel. *Surgery* 69(2):288-293, 1971.

The pathology of juvenile polyps of the colon was investigated in a series of 55 patients, who had a total of 89 polyps of the juvenile type. These polyps were round or oval and were attached to a slender stalk; they were composed primarily of fibrous stroma usually infiltrated with acute and chronic inflammatory cells. Neither adenomatous polyps nor familial polyposis polyps were seen. No malignant potential was shown by any polyp. The age of patients with polyps ranged from 2-27 yr, with peak numbers of cases occurring in the 3-5 yr age group (7-9 cases); after age 9, there was a sharp decline in the numbers of polyp patients. Most polyps were located within the rectum. The findings fail to confirm the hypothesis that the juvenile polyp is a stage in the development of the adenomatous polyp.

1592 PATHOGENESIS OF THE MUCOSAL FOLDS ASSOCIATED WITH EARLY CARCINOMA OF THE RECTUM. (Fr.) Parturier-Albot, M. (Hotel-Dieu, Paris, France) and G. Albot. *Sem Hop Paris* 47(8):485-493, 1971.

Certain deformities of the mucosa around cancers of the rectum are described, which may be useful in determining malignancy at an early stage. The most important perilesional modifications for early diagnosis resembled those seen in small gastric cancers, with rigid sections presenting the classical aspects of infiltration, encystment, and areas of semi-rigid texture. These modifications, however, were not due to the tumor formation but to a concomitant sclerosis of the submucosa and were thought to be responsible for the appearance of abnormal folds in the mucosa, the granular character of the mucosa, and irregular folds, either thickened or containing polypoid features. Aside from the classical proctological examination by means of endoscopy, biopsy specimens were examined by serial section, and it was possible to demonstrate that as the tumor developed the early signs disappeared. The early signs

were considered to be due to vasomotor disturbances and related to contractions of the muscular mucosa.

- 1593 MALIGNANT NEURINOMAS OF THE GASTROINTESTINAL TRACT: REMARKS ON THEIR PATHOGENESIS. (Ger.) Köthe, W. (Path. Inst. U. Heidelberg, Germany). *Äertal Forsch* 25(1):20-26, 1971.

Solitary malignant neurinomas are described in 4 cases and problems related to histogenesis are considered. The first case was characterized by a tendency to infiltration with small variations in the nuclear size and rare mitoses; the second, by a regression in polar structure (Type Antoni A); the third again showed typical histological structures of Type Antoni A, with a tendency for tumor infiltration; and case 4 represented the highest degree of change including infiltration and necrotic formation. The malignant neurinomas appeared to originate from Schwann cells and the peri- and endoneural fibrocytes had a common Schwann-like mother cell, which later can become the matrix for tumor cells if their maturation is disturbed or inhibited, as is characteristic of von Recklinghausen's disease. In the malignant neurinomas tissue structures similar to those in von Recklinghausen's disease, were found. Well-differentiated Schwann cells were found in the Antoni A type polar structures, and were less differentiated in the reticular tissue.

- 1594 PATHOGENESIS OF EXPERIMENTAL HORMONE-PRODUCING OVARIAN TUMORS. (Rus.) Sheykin, P. I. (Med. Inst. Donets, U.S.S.R.). *Vop Onkol* 16(11): 48-54, 1970.

The administration of chorionic gonadotropin to random-bred rats following a single exposure of irradiation (1000 r) produced no effects on ovarian tumor incidence, latency period or morphology. The hormone was injected s.c. (100-150 U/rat) for 5 days a week over a 1-9 month period starting 3, 9 or 13 months following radiation exposure. The incidence of ovarian tumors (first occurring 11 months after radiation exposure) was 62% with respect to surviving rats and 12% with respect to the initial number of 435 rats. Androblastomas were the most frequently occurring tumors, with an incidence of 49% among the irradiated rats and 62% among the gonadotropin-treated rats. Luteomas occurred in 19% of the irradiated and in 14% of the hormone-treated rats. Thecal and granular thecal cell tumors were noticed along with the luteocellular neoplasms. Chorionic gonadotropin exhibited no luteotropic effects on the development of ovarian tumors which indicates that the intraovarian endogenous factor is more important in all the stages of the neoplastic process.

- 1595 CANCEROUS AND PRECANCEROUS STATES OF THE CERVIX UTERI: A HISTOLOGICAL AND HISTOCHEMICAL STUDY. (E.) Stenback, F. (Dept. Path. U. Oulu, Finland), A. Ojala and A. Vehaskari. *Acta Obstet Gynec Scand* 49(4):389-397, 1970.

Histochemical features of the transition from non-malignant to invasive malignant states of the cervix

uteri were investigated in 100 unselected biopsy specimens; specimens were examined for the presence of 13 chemical substances, and 27 additional specimens were examined for the presence of 9 enzymes. Specimens were classified as normal, dysplasia grade 1, dysplasia grade 2, carcinoma *in situ*, invasive well-differentiated carcinoma, and anaplastic carcinoma. As compared to normal cervical tissue, dysplasia grades 1 and 2, and carcinoma *in situ* showed relatively slight glycogen staining; well-differentiated and anaplastic carcinoma also showed decreased stainability of glycogen. Stainability of RNA was higher in dysplasia grades 1 and 2 than in normal tissue, and higher in carcinoma *in situ* and well-differentiated carcinoma than in dysplasia. Anaplastic carcinoma showed stainability of RNA comparable to that of dysplasia grade 1. Lactate dehydrogenase activity also increased with increasing malignancy and was maximal in well-differentiated carcinoma, lower in anaplastic carcinoma, and minimal in normal tissue. The histochemical changes reflected a disturbance in the normal differentiation of cells from basal to parabasal and superficial cells; the production of abnormal cell forms tending to pathological keratinization was also seen to accompany increasing malignancy.

- 1596 CYTOLOGICAL FEATURES OF PRECANCEROUS CONDITIONS AND CANCER OF THE UTERINE CORPUS. (Rus.) Kazanova, L. I. (Inst. Exper. and Clin. O Acad. Med. Sci., U.S.S.R.), V. I. Peskova and A. Kurbanova. *Lab. Delo* 12:733-737, 1970.

The cytological features of endometrial cells in uterine cancer, recurrent hyperplasia or endometrial polyposis were investigated in 44 patients (31 with uterine cancer and 13 with glandular hyperplasia or endometrial polyposis) 33-78 yr of age. Small average size cells with well-defined boundaries and round or oval central nuclei were seen in polyposis; chromatin was regularly distributed and Barr bodies were found in 30-40% of the cells. Enlarged cells with oval, round or rod-like nuclei with well-defined membranes were observed in hyperplasia; chromatin was regularly distributed within the nucleus, and 8 of 10 patients had Barr bodies in 24-42% of the tumor cells. Preparations from patients with recurrent hyperplasia of the endometrium showed polymorphic cells with oval or prismatic nuclei and regular chromatin distribution; intense epithelial proliferation with considerable cell atypia was observed and was considered to be an early stage of malignancy; Barr bodies were found in 15-17% of the cells. Fifteen of 31 cancer patients had Barr bodies in more than 20% of the cells and 11 had Barr bodies in 10-19% of the cells. 5 patients had sex chromatin-negative tumors (sex chromatin was present in less than 10% of the cells). The latter tumors consisted mainly of anaplastic while all sex-chromatin-positive tumors appeared to be adenocarcinomas.

- 1597 CLUES TO THE POSSIBLE MODE OF ACTION OF CIGARETTE SMOKE IN THE PATHOGENESIS OF CANCER. (E.) Malhotra, S. L. (Med. Dept., South Railway, Garden Reach, Calcutta, India). *J Indian Med Ass* 55(8):265-270, 1970.

Tobacco smoke from various sources, including cigarettes, pipes, and cigars, was tested to determine whether, and in what degrees, smoke from each source neutralized HCl and NaOH; the results were discussed in relation to possible etiological factors for human lung cancer. It was found that tobacco smoke did not neutralize HCl, and that pipe smoke was more acidic than cigarette or cigar smoke. The amounts of tobacco smoke neutralized by 0.32N NaOH were 7.3, 6.9, 5.3, 4.7, 1.6 and 2.1 ml, resp., for 6.7 g of cigarette paper, pipe, Indian *biris*, cigar, unfiltered cigarettes, and filtered cigarettes, resp. Pipe tobacco smoke was found to contain more CO₂ than did smoke from other tobaccos. These findings correlated with changes of the respiratory epithelium thought to result from the action of weakly acidic smoke, such as loss of intracellular mucus from epithelial tissues leading to inflammatory and proliferative changes in the mucosa. These effects of cigarette smoke on intracellular mucus were thought to be more pronounced in persons with unusually high numbers of mucus-bearing goblet cells, and less pronounced in persons with fewer goblet cells and more non-mucus-bearing ciliated cells.

1598 PRIMARY LIVER CANCER DEVELOPED FROM CIRRHOSIS. (Fr.) Caroli, J. (Hosp. St. Antoine, Paris, France), N. Marcus, A. Grynblat and B. Chevrel. *Rev Medicochir Mal Foie* 45(6):291-298, 1970.

1599 THE PERILESIONAL MUCOSA INDICATIVE OF EARLY RECTAL CARCINOMA: ITS SIGNIFICANCE AND THE HISTOLOGICAL FINDINGS. (Fr.) Parturier-Albot, M. (Coll. Med. Hosp. Paris, France) and G. Albot. *Ann Med Intern* 121(12):1001-1008, 1970.

1600 SQUAMOUS CELL EPITHELIOMA OF THE RENAL PELVIS DUE TO CORAL CALCULUS. (Ger.) Zielinski, J. (Urol. Clin. Katowice, Poland), M. Luciak and J. Czopik. *Z Urol* 63(12):883-890, 1970.

1601 GARDNER'S SYNDROME: AN UNUSUAL ETIOLOGICAL FACTOR IN THE DEVELOPMENT OF MAXILLAR TUMORS. (Fr.) Gosserez, M. (Nancy, France), A. Treheux, J. C. Hoeffel, M. Stricker, J. Fays and F. Valentin. *J Radiol Electr* 51(8-9):503-506, 1970.

See also:

- * (Rev): 1282
- * (Chem): 1299, 1323, 1329, 1350
- * (Phys): 1406
- * (Viral): 1516
- * (Path): 1586
- * (Epid-Biom): 1620, 1624

- 1602 CANCER STATISTICS, 1971. (E.) Silverberg, E. (Amer. Cancer Soc., New York, N. Y.) and A. I. Holleb. *CA* 21(1):13-31, 1971.

Changes in recording, classifying and compiling cancer mortality statistics since 1914 are discussed, emphasizing the particular problems of data interpretation which these changing policies have created. Figures for estimated 1971 cancer deaths adjusted for sex and site are presented together with estimated 1971 figures for cancer incidence for sex and site. Statistics from 1967 on cancer death rates for various sites among males and females in the United States and statistics on trends in age-adjusted cancer death rates from 1950-1952 and from 1965-1967 are reported. Estimates for 1971 by state for cancer deaths for all sites and global age-adjusted death rates from cancer of all sites from 1964-1965, are included.

- 1603 ACUTE CHILDHOOD LEUKEMIA: EPIDEMIOLOGIC STUDY BY CELL TYPE OF 1,263 CASES AT THE CHILDREN'S CANCER RESEARCH FOUNDATION IN BOSTON, 1947-1965. (E.) Fraumeni, J. F. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), M. D. Manning and W. J. Mitus. *J Nat Cancer Inst* 46(3):461-470, 1971.

Forty-four percent of 1,263 children under 15 yr with acute leukemia had lymphocytic leukemia, 24% had undifferentiated leukemia, 24% had myelogenous leukemia, and 8% had monocytic leukemia. More boys than girls had acute leukemia generally; lymphocytic and undifferentiated leukemia had maximal incidences at age 3-4 (120 and 60 cases, resp.). Monocytic leukemia had its maximal occurrence at less than 1 yr-of-age, and declined in incidence thereafter. Lymphocytic and undifferentiated leukemia declined in incidence after age 4-5 yr; after age 9 the predominant type of leukemia was myelogenous. Survival was most prolonged for children with lymphocytic leukemia (33 months after diagnosis), and shortest for children with monocytic leukemia (13 months after diagnosis). Down's syndrome occurred in 14 of the 1,263 children, which is 7 times in excess of that for the larger society. The excess of Down's syndrome was associated with all cellular types of leukemia. Other congenital defects observed in the childhood leukemia patients included Fanconi's anemia, Marfan's syndrome, and familial ectodermal dysplasia. There were 28 twins among the leukemia patients; 1 set of male twins had monocytic leukemia. Two pairs of male sibs (non-twin) had lymphocytic leukemia.

- 1604 CATS AND CHILDHOOD LEUKEMIA. (E.) Bross, I. D. J. (Roswell Park Mem. Inst., Buffalo, N. Y.) and R. Gibson. *J Med Exp Clin* 1(3):180-187, 1970.

Three hundred families in which a case of childhood leukemia had occurred and 831 randomly-selected families were examined to determine whether exposure to cats was causally related to childhood leukemia. Relative risk of leukemia associated with exposure to each of 15 animals was estimated, with the result that the relative risk associated with cats was 1.35; maximum relative risks were associated with geese (1.80), and minimum risks were associated with guinea-

pigs (0.81). Cats were the only animal with relative risk significantly exceeding 1 which were associated with a large number of leukemia cases; 117 leukemia cases were recorded as having been exposed to cats (38.1% of leukemia cases). Thirty-one percent of normal families were recorded as having been exposed to cats. More leukemia cases had been exposed to or dead cats than controls; 13% of children aged 1 yr with leukemia had been exposed to sick or dead cats compared with 6.5% of control children. The age-adjusted relative risk of leukemia development for children exposed to sick or dead cats was 2.24. These results were thought to provide evidence that exposure to cats, especially to sick cats, may be a causal factor in the development of leukemia in children. However, only about 1 case of childhood leukemia in 100,000 appeared to be accounted for by exposure to cats.

- 1605 THE EPIDEMIOLOGICAL IMPORTANCE OF CHILDHOOD CANCERS. (E.) Stewart, A. (Dept. of Med., U. Oxford, England) and R. Barber. *Brit Med Bull* 27(1):64-70, 1971.

Contributions to the understanding of carcinogenesis made by the Oxford Survey of Childhood Cancers are described. The Survey has collected data indicating that prenatal X-irradiation is associated with a general hazard of cancer development of various sites, and is not confined to an increased risk of leukemia development. A national increase in leukemia mortality in England and Wales in 1950-1959 did not affect children under 2 yr-of-age to the degree that it affected older children; there were 65 leukemia deaths/10⁶ children aged 3 yr and only 28 deaths/10⁶ children aged 2 yr. The relatively low incidence of leukemia deaths in children under 2 yr-of-age was thought to be due to the long latent period for leukemia (3-6 yr); it was also suggested that a decline in the death rate from pneumonia among children might have produced an apparent rise in the mortality rates from other conditions, including leukemia. The survey showed that children are more cancer prone than young adults, casting doubt on the accepted theory that cancer susceptibility increases with age from birth. The discovery that prenatal diagnostic X-irradiation had different carcinogenic effects postnatal irradiation (e.g., atomic bomb irradiation) may indicate that "the cell conversion phase" of the cancer process is achieved more easily than the first step in the cell-multiplication phase, phase.

- 1606 DEATHS FROM CHILDHOOD LEUKEMIA AND SOLID TUMORS AMONG TWINS AND OTHER SIBS IN THE UNITED STATES, 1960-1967. (E.) Miller, R. W. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *J Nat Cancer Inst* 46(1):203-209, 1971.

Cancer mortality among twins and other sibs was surveyed from 1960-1967 in the United States. Several pairs of identical twins were found to have died of leukemia in this period; in the case of all but 1 of the twin pairs, the deaths were separated by less than 8 months and occurred in the first 6 yr of life. The concordance rate for leukemia in

twins was therefore maintained at about 17%. Eight brain tumors were found among non-twin sibs (as opposed to 0.9 expected cases). Leukemia among non-twin sibs was not concentrated in the first 6 yr of life and did not affect both sibs at the same age. There were 8 families in which 1 sib died of brain tumor and another of cancer of the bone or muscle. In 2 families, 1 sib had adrenocortical carcinoma and another had rhabdomyosarcoma, a combination which may represent part of a familial cancer syndrome. Of 3 sibs with lymphoma and 1 with lymphocytic leukemia, each had sibs with carcinoma of the colon; in 1 case, the colon cancer was associated with polyposis. Wilm's tumor, lymphoma, and neuroblastoma were also recorded for sib sets.

1607 HODGKIN'S DISEASE IN ENGLISH AND AFRICAN CHILDREN. (E.) Burn, C. (Albany Med. Coll., N. Y.), J. N. P. Davies, O. G. Dodge and B. C. Nias. *J Nat Cancer Inst* 46(1):37-41, 1971.

The distribution of symptom types of Hodgkin's disease in children from 3 East African countries and from the Manchester, England vicinity were compared. African children had a significantly higher incidence of the lymphocytic depletion type of Hodgkin's disease than did the English children. Eight percent of Manchester male children and 12% of Manchester female children had lymphocytic depletion compared to 34% of African males and 57% of African females. In Manchester, there were 37 male cases and 16 female cases, while in Africa there were 112 male cases and 21 female cases. African children also had a higher proportion of lymphocytic depletion lesions than children studied from France and from Texas.

1608 CANCER IN AFRICA. (E.) Cook, P. J. (U. Coll. Hosp. Med. Sch., London, England) and D. P. Burkitt. *Brit Med Bull* 27(1):14-20, 1971.

The incidence of carcinoma in 7 selected sites in Negro populations in Africa south of the Sahara was investigated. Primary cancer of the liver was found to be the most common of all forms of cancer, representing 10-30% of all tumors in males throughout sub-saharal Africa. Its frequency in Africa is as much as 1000 times higher than its frequency in Europe. Dietary aflatoxins may be an etiological factor for liver cancer in Africans. Esophageal cancer shows more local variation of frequency than any other tumor in Africans, being rare in West Africa and very common in parts of East and South Africa. Heavy use of alcohol in which nitrosamines may be present is implicated in the incidence of cancer of the esophagus in Africa. Stomach cancer is frequent in western Kenya, and rare in northern Uganda; there may be a correlation between the high incidence and altitude. Cancer of the penis is of low frequency in East Africa where circumcision is traditional, and of high frequency west of the Kenya-Uganda border where circumcision is uncommon. Cancer of the cervix uteri is the commonest cancer in females in tropical Africa, representing 20-40% of all tumors in most series. The frequency of this condition is far higher in Africa than in western Europe and North America. It

is widespread throughout sub-saharal Africa. Kaposi's sarcoma is almost confined to Africa, representing almost 16% of male tumors in East Africa. Areas of high concentration include western Uganda. Bladder tumors are especially common in Malawi, where they represent more than 18% of all female tumors. Evidence exists for an association between cancer of the bladder and urinary bilharziasis. The development of epitheliomas on scars left by tropical leg ulcers is common in Africa and showed little regional variation in distribution. Burkitt's lymphoma distribution in Africa may be correlated with rainfall and temperature and may involve an insect vector tentatively identified as the mosquito which transmits malaria. The rarity of intestinal cancer in Africa mirrors its rarity in other underdeveloped rural areas, and may be related to cellulose content of the local diets.

1609 RACIAL VARIATIONS IN TUMOR INCIDENCE IN UGANDA. (E.) Templeton, A. C. (Dept. Path., Makerere U. Coll., Kampala, Uganda) and O. A. C. Viegas. *Trop Geogr Med* 22(4):431-438, 1970.

The incidence of cancer at various sites was determined for the African, Asian and European population groups in Uganda. While age-specific incidence rates rose for all 3 populations with age, the incidence of malignant disease dropped off in Africans at the age of 70 yr, while in Asians and Europeans it continued to rise after this age. Cancer of the oral cavity was seen most often in Asians (5.7% incidence); the high incidence of this condition may have been related to the Asian habit of chewing betel and tobacco. Asians and Europeans had higher rates of cancer of the colon, rectum and anus than Africans, possibly due to dietary differences between the Africans and the other groups. The incidence of liver cell carcinoma was higher in Africans than in the others; aflatoxin consumption may be responsible. Asians and Europeans in Uganda had higher incidences of bronchial carcinoma than did Africans; cigarette smoking and industrial pollution were thought to be the relevant etiological factors. Europeans had the highest rates of mammary cancer, and Africans had the lowest rates. Ugandan Africans had higher rates of cervical cancer than Ugandan-resident Asians or Europeans. Europeans had a markedly higher incidence of skin cancer than Africans or Asians in Uganda; exposure to sunlight was thought to be importantly related to cancer of the skin. Asians had higher rates of leukemia than Africans or Europeans. In general, environmental factors were thought to be more important than genetic factors in determining the differential rates of cancer in the 3 Ugandan populations under study.

1610 EPIDEMIOLOGY OF ASBESTOS CANCERS. (E.) Wagner, J. C. (Llandough Hosp., Penarth, Glamorgan, Wales), J. C. Gilson, G. Berry and V. Timbrell. *Brit Med Bull* 27(1):71-76, 1971.

The correlation between bronchial and pleural cancer and occupational exposure to asbestos was investigated in a survey of the literature from several countries. Mortality rates from chrysotile-mining

areas in Rhodesia and Swaziland do not show excesses in mortality from pleural or bronchial cancer; however, in the Cape Province where crocidolite is mined, significant excesses of pleural and peritoneal mesothelioma have been recorded for people living and working near the asbestos mines. In Britain, all groups of mesothelioma with case controls showed significant association with exposure to asbestos; decreases in risks of bronchial cancer have been shown to coincide with increasingly effective dust-control measures in British industries using asbestos. Similar findings have been reported from the United States. In Quebec, asbestos mining (chrysotile) has not been found to involve increasing incidence of mesothelioma. Small increases in mortality from bronchial cancer have been found for anthophyllite and other asbestos miners in Finland and Sweden. In general, it appears that an association between asbestos exposure and bronchial cancer and mesothelioma of the pleura and peritoneum is well established. The risk of bronchial cancer seems to be more clearly related to the intensity of past exposure and to the risk of asbestosis. Cigarette smokers who are exposed to asbestos are at much higher risk of developing bronchial cancer than are nonsmokers. Mesothelioma is less clearly related than bronchial cancer to dose of asbestos exposure.

- 1611 EFFECT OF CIGARETTE SMOKING ON CONNECTICUT RESIDENTS. (E.) Christine, B. W. (Conn. St. Hlth. Dept.) and P. D. Sullivan. *Connecticut Hlth Bull* 85(1):23-28, 1971.

The incidence of malignant diseases associated with cigarette smoking in Connecticut was investigated. Heart disease and cancer, the leading causes of death in the state as in the nation, have accounted for increasing numbers of deaths in recent yr. The rate of deaths from heart disease in 1925 in Connecticut was 179.1 deaths/100,000 population and 336.6/100,000 in 1969. Cancer of the respiratory system in Connecticut had an incidence of 14 cases/100,000 in 1935 among males and 70 cases/100,000 in 1970; among Connecticut females, the increased incidence has not been marked, with the incidence/100,000 cases being 5 in 1935 and 9 in 1970. Cancer (all sites) accounted for 272 deaths among Connecticut residents in the 25-44 yr age group in 1969 and 1,843 and 2,894 deaths in the 45-64 yr and 65 yr age groups, resp. Cancer of the larynx has shown a steadily increasing percentage of cases in males (66.4% in 1965 and 71.9% in 1966). Males in Connecticut have also showed increasing rates for cancer of the esophagus and bladder, which are 2 other sites of cancer thought to be causally related to cigarette smoking.

- 1612 CANCER OF THE LIP IN CONNECTICUT, 1935-1959. (E.) Shedd, D. P. (Roswell Park Mem. Inst., Buffalo, N. Y.), C. F. Von Essen, R. R. Connelly and H. Eisenberg. *Cancer Bull* 22(6):116-120, 1970.

The incidence and pathology of cancer of the lip in Connecticut residents was investigated in a survey of 1,255 patients. Men comprised 1,178 of the patients, and 1,089 of these showed involvement of the lower lip. Thirty-nine percent of women with

lip cancer had involvement of the upper lip. The mean age at diagnosis was 64 yr for men, and 67 yr for women. The incidence of lip cancer among men increased steadily with age; numbers of cases/100,000 population for men aged 40 and 55 yr were 4 and 10, resp. For women, numbers of cases/100,000 population at ages 40 and 55 yr were 0.5 and 1, resp. Eighty-one percent of lip cancer cases were diagnosed as squamous cell carcinoma. Six men and 2 women presented with carcinoma *in situ*, but most patients were in the stage of disease in which the cancer was active but localized to the lip. The 5 yr survival rate for all lip cancer patients was found to be 86%. Men with lip cancer were found to have a survival advantage over women.

- 1613 A STUDY OF LEUKEMIA WITHIN THE WEST GERMAN ARMED FORCES. (E.) Altwein, J. (Inst. Path. West German Armed Forces, Olpenitz), U. B. Mairose and K. W. Wegner. *Milit Med* 136(3):238-241, 1971.

The incidence, mortality and pathology of leukemia were investigated in the Army of the German Federal Republic between the yr 1956-1969, during which time there were 66 deaths from leukemia. The subjects ranged in age from 18-60. Mortality from leukemia ranged from 0 deaths/100,000 military personnel in 1956 and 1957 (when the Army was of limited size) to 3.2 and 2.5 deaths/100,000 in 1960 and 1969, resp. Frequency of leukemia was highest in the 20-25 yr group with peaks at the age of 21 yr (9 cases); a lower peak was recorded for the 55 yr group (3 cases). Fifty percent of acute leukemias were diagnosed within 1 month from the onset of symptoms, and 2 months thereafter 50% of the patients were dead. Possible etiological factors in leukemia cases revealed by case histories included exposure to radioactive material for 3 yr, and exposure to dimethylformamide and polyacrylonitrile. One patient's sister had chronic myelogenous leukemia. Leukocytosis of above 100,000/mm³ was observed in 25% of the patients at the time of hospital admission, but 33% showed normal or near-normal leukocyte counts.

- 1614 MELANOMA IN UTAH. (E.) Cowan, L. B. (Salt Lake City, Utah), C. R. Smart and V. Moslander. *Rocky Mountain Med* 68(1):29-32, 1971.

The incidence of melanoma in the state of Utah was surveyed for the period 1957-1970. In that time, there were 282 cases of melanoma recorded in the state, including 54% males and 46% females. Ninety eight percent of cases were among Caucasians (the Negro population of Utah is negligible). While only 15 cases of melanoma were reported in 1957-1958, 90 cases were reported in 1968-1969; the increase probably represents the increased efficiency of the central cancer registry serving 5 western states including Utah. Thirty-six percent of the melanomas affected the limbs, 31% affected the head and neck, and 21% affected the trunk. Melanoma was found to be rare in childhood, and its frequency increased with puberty and reached maximum levels at 50-55

yr-of-age. Five-yr survival figures indicated that 70% of patients with localized melanoma survived for 5 yr from diagnosis; 41% of patients with regional disease survived for 5 yr.

1615 A NOTE ON THE INCREASED RISK OF POLYCYTHEMIA VERA IN JEWS. (E.) Modan, B. (Tel Hashomer Govt. Hosp., Israel), H. Kallner, D. Zemer and C. Yoran. *Blood* 37(2):172-176, 1971.

The incidence of polycythemia vera among Jews born in Israel and Jews born in Africa and Asia was investigated in the Israeli population. Records of polycythemia vera from the period 1955-1966 revealed 155 newly diagnosed cases of definite polycythemia vera and 27 probable cases. The mean annual incidence yielded by these figures was 6.7 cases/million (7.8 including probable cases). The male:female ratio was 1.1:1; however, after the age of 50 yr, incidence was higher among females. In both sexes, there was a peak incidence in the 60-69 yr age group. In both sexes, incidence of polycythemia vera was markedly higher in European-born Jews than in Asian-African born Jews; among males aged 60-69 yr, European-born Jews had an incidence of 37.3/million, while Asian and African-born Jews had an incidence of 11.1/million. The reason for the relatively high incidence of polycythemia vera among European-born Israeli Jews is unclear.

1616 BILIARY CANCER AMONG SOUTHWESTERN AMERICAN INDIANS. (E.) Rudolph, R. (U. Hosp. Cleveland, Ohio), J. J. Cohen and R. H. Gascoigne. *Arizona Med* 27(10):1-4, 1970.

The incidence and pathology of biliary tract cancer among American Indians in New Mexico was investigated. Carcinoma of the gallbladder was found in 35 cases and cancer of the extra-hepatic bile ducts in 7 cases of 748 operations performed on the gallbladder and/or bile ducts. These findings yielded incidences for gallbladder cancer and ductal cancer of 4.5% and 0.9%, resp., which are well in excess of the figures found for the population at large, which have been estimated at 2% for gallbladder cancer and 0.5% for duct cancer. Cancer of the bile ducts and gallbladder comprised 9% of all digestive system malignancies for the New Mexico Indian population. The average age of gallbladder cancer patients was 67 yr and 64 yr for ductal cancer. In the former group, there were 9 men and 26 women; in the latter, there were 4 men and 3 women. Thirty-five patients were Navajos, 6 were Zunis, and 1 was Hopi. Adenocarcinoma was the pathologic diagnosis in all cases; the most consistent blood chemistry finding for the patients was a prothrombin time exceeding 13-14 seconds; the second most frequent feature was an elevated bilirubin. The proportion of gallbladder cancer patients surviving 5 yr after diagnosis was 9%.

1617 REGIONAL CONVERGENCE OF CANCER MORTALITY RATES OVER TIME IN THE UNITED STATES, 1940-1960. (E.) Waggoner, D. E. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.) and G. R. Newell. *Amer J Epidemiol* 93(2):79-83, 1971.

Regional variation in cancer mortality was investigated to pursue an earlier finding that cancer mortality was negatively correlated with environmental temperature. A general stability of high correlation between mortality and temperature through 2 decades was observed, with 3 exceptions. Cancer of the respiratory system showed a decreasing relationship with temperature; the high negative correlation in men for leukemia mortality and temperature appeared to have declined, and a low positive relationship with temperature was found in females. Finally, a continued negative correlation was found between temperature and buccal cavity and pharyngeal cancer for males. In all cancer sites, the relative variance among regions decreased from 1940-1960. Regions with relatively low site-specific death rates showed the largest percent increases in mortality rates from 1940-1960. Regional cancer rates in some parts of the nation appear to be converging toward overall national levels.

1618 BREAST CANCER IN AN AREA OF HIGH PARITY: SAO PAULO, BRAZIL. (E.) Mirra, A. P. (Central Cancer Registry, Sao Paulo, Brazil), P. Cole and B. MacMahon. *Cancer Res* 31(2):77-83, 1971.

The correlation of risk of developing mammary cancer with age at first pregnancy and with other variables was studied in a survey of 536 cancer cases and 1550 controls in Sao Paulo, Brazil. A statistically significant relationship was found between high risk of developing breast cancer and schooling; women with no schooling had a risk of 1.0, while women with 8-11 yr of schooling had a risk of 1.8. Women who had their first pregnancy before the age of 20 yr were found to have only about 2/3 the risk of developing breast cancer incurred by women whose first pregnancy had occurred at the age of 25 yr or later; a protective effect in both groups was observed for each parity level, indicating that the association of mammary cancer risk with age at first pregnancy was not merely a reflection of the well-known phenomenon of low cancer risk for women of high parity. The protective effect of early pregnancy was confined to women under the age of 50 yr. A correlation between risk of contracting breast cancer and increasing wt or wt/height index was seen in women above 50 yr. The relative risk of mammary cancer was 1.6 for women over 50 weighing 55-64 kg and 2.5 for women over 50 weighing over 75 kg. There was no appreciable difference in lactation patterns between cancer patients cases and controls.

1619 CANCER MORTALITY: PERSPECTIVES AND GYNECOLOGIC CANCER. (E.) Floyd, W. S. (Sinai Hosp., Detroit, Mich.). *Bull Sinai Hosp Detroit* 19(1):19-21, 1971.

The incidence in the United States of female genital cancers was discussed. Cancer is the leading cause of death among women aged 35-70, with 24,000 cancer deaths in this age group estimated to have occurred in 1970. Of these deaths, 9,400 will result from cancer of the cervix uteri, 3,500 from cancer of the corpus uteri, and 10,000 from ovarian cancer. The Papanicolaou smear test has reduced

the mortality from uterine cancer by 50% during the past 25 yr; however, the death rate for cancer of the ovaries has more than doubled in the past 30 yr (from 3.5 deaths/100,000 females in 1930 to 10 deaths in 1970). An increased use of cytologic screening might further improve the mortality from female genital cancers.

- 1620 FACTORS RELATED TO PROGRESSION OF CERVICAL ATYPIAS. (E.) Hulka, B. S. (Sch. Publ. Hlth., U. North Carolina, Chapel Hill) and C. K. Redmond. *Amer J Epidemiol* 93(1):23-32, 1971.

The probability of progression from an atypical cytological cervical cancer smear to a more serious cytologic and histologic status was investigated in a cervical cancer screening program involving 402 women with atypical smears on initial screening and 168 women with atypical smears on a subsequent screening. The probability of progression from an atypical smear discovered on first screening to a more serious condition was found to be greatest in the first 6 months after the first diagnosis of cytological atypia, the probability of progression during this period amounting to 13.6%. After 1 yr following initial discovery of atypia, the probability of progression remained constant and was approximately 3-4% in each 6-month interval. The cumulative probability of progression during the first 5 yr after initial screening was 41.2%. The highest probability of progression for an atypical smear taken on the 2nd to the 5th screening was recorded during the first 6 months after the finding of the initial atypia and amounted to 7.7%. The cumulative probability of progression for these smears reached its maximum in 2½ yr (17.6%). The semi-annual progression rates for smears discovered to be atypical on first screening was about half that of smears discovered to be atypical on subsequent screenings. Among women less than 30 yr-of-age, whites had a greater probability of progression than Negroes. Generally, progression rates were high among women 30-44 yr, and low in Negroes below 30 yr. Two other variables found to have some association with progression among white women were numbers of pregnancies and numbers of deliveries; increasing numbers of either were associated with increased progression rates, but not to the degree of statistical significance.

- 1621 INCIDENCE OF MULTIPLE PRIMARY CANCERS: IV. CANCERS OF THE FEMALE BREAST AND GENITAL ORGANS. (E.) Schottenfeld, D. (Mem. Hosp. Cancer Allied Dis., New York, N. Y.) and J. Berg. *J Nat Cancer Inst* 46(1):161-170, 1971.

The incidence of multiple primary cancers of various organs in women with carcinomas in the breast or genital organs was investigated in a survey of 9,792 breast cancer patients and 4,363 cases of cancer of the genitalia. Among the breast cancer patients, there were 58 synchronous and 248 metachronous primary cancers in the opposite breast, yielding an incidence of 6.1 metachronous primary cancers in the opposite breast/1,000 patients/yr. This incidence was 4.5 times the expected incidence of metachronous primary

opposite breast malignancies. Among women with carcinomas of the breast, the incidence of multiple primary cancers in the ovary was 0.6/yr/1,000 patients. This incidence was only 1/10 of the risk of developing opposite breast malignancies, but was twice the expected risk of developing ovarian cancers. Among women with primary ovarian cancers, the incidence of metachronous primary breast cancers was 5.3/yr/1,000 patients, or 4.4 times the expected rate. The observed number of subsequent cancers of the corpus uteri was less in women with primary breast carcinomas than in women with ovarian cancers. Among women with primary cancers of the corpus uteri, the incidence of breast cancers was 3.2/yr/1,000 patients, or 2 times the expected rate. The risk of developing a subsequent breast cancer for women with endometrial cancer was 1.25-2.0 times the normal risk. Three of the 5 multiple primary soft tissue sarcomas developed as sequelae to previous breast cancers. It appeared that the positive association of multiple primary carcinomas of the breast, ovary and endometrium represented demographic and etiologic factors common to these conditions.

- 1622 THE EPIDEMIOLOGY OF MALIGNANT TUMORS. (It.) Susanna, L. (Inst. Hyg., U. Pavia, Italy), A. Marinoni and E. Lanzola. *Ig Sanit Publ* 26(7-8):269-282, 1970.

An increase in death rate from cancer from 1.1% to 1.9% within the last 10 yr was observed in the province of Bergamo. The cancer incidence was 2.3% in males and 1.6% in females. The populations living in industrial areas had a higher cancer incidence than those from rural areas; this difference appeared to be most visible among populations above 50 yr-of-age (4.6% vs. 3.5%, resp.). The urinary tract, the genital organs, the lung, intestine and liver appeared to be among the organs most susceptible to neoplastic development. No significant differences related to the altitude of the populated areas (excluding the industrial areas) were seen in tumor incidence; however, there seemed to be a decrease in cancer mortality with decreasing altitude.

- 1623 INCIDENCE OF BRONCHOGENIC CARCINOMA IN NEGROES: STATISTICAL ANALYSIS OF 94 CASES. (E.) Rickard, V. D. (Dept. Path., Howard U., Washington, D. C.) and C. C. Sampson. *J Nat Med Ass* 63(1):10-12, 1971.

The pathology of bronchogenic carcinoma in the American Negro was investigated in a study of 94 patients. Seventy-five were male, and 19 were female; 37 were aged between 51-60 yr, 33 were aged between 61-70 yr, and 15 were aged between 41-50 yr. Squamous cell carcinoma was the most common diagnosis (45.7% of cases), followed by undifferentiated carcinoma (40.4%). More females had undifferentiated carcinoma than any other type of lesion, while squamous cell carcinoma was the predominant pathologic type among males. A relationship was found between development of bronchogenic carcinoma and cigarette smoking. The incidence of carcinoma was 40% greater in smokers of more than 1 pack/day than in nonsmokers. Of 63 smoking pa-

patients, 27 developed squamous carcinoma, 23 developed undifferentiated carcinoma, and 7 developed adenocarcinoma.

1624 EPIDEMIOLOGICAL STUDY OF PRECANCEROUS LESIONS OF THE ORAL CAVITY: A PRELIMINARY REPORT. (E.) Mahi, P. N. (Indian Counc. Med. Res., New Delhi), V. P. Mital, B. Lahiri, U. K. Luthra, R. K. Seth and G. D. Arora. *Indian J Med Res* 58(10):1361-1391, 1970.

A survey of 534 cases of oral and oropharyngeal carcinoma, representing 7% of the screened population of Mainpuri district (India) revealed that leukoplakia was the predominant form of oral-oropharyngeal cancer in this population. Male cases were found to outnumber female cases by more than 3 to 1. The rate of oral-oropharyngeal carcinoma increased with increasing age, 44 cases occurring in the 35-39 yr group and 70 cases occurring in the 50-54 yr group. Hindus had a higher incidence of leukoplakia and submucous fibrosis than Muslims, and cultivators, laborers and "skilled workers" had significantly higher rates of oral-oropharyngeal cancer generally than did other occupational groups. Median income groups and groups having relatively high levels of education showed increased frequencies, persons with a "primary" education having prevalence rates of 163.3 and illiterate persons having rates of 46.9. Tobacco chewing was highly correlated with incidence of leukoplakia; the risk for this condition was 62 times higher in daily tobacco-chewers than in non-chewers. Those acquiring the tobacco chewing habit early in life were at greater risk of developing precancerous lesions of the oral cavity than those who began to chew tobacco at a later age. Increased risk of developing oral-oropharyngeal cancer was higher in those who chewed tobacco for 200 min/day or longer than for those who chewed tobacco for less than 200 min/day. Higher risks for oral-oropharyngeal precancerous lesions were associated with the use of chewing tobacco compounded of tobacco, betel, clove and lime than with the use of pure chewing tobacco. Tobacco smoking also predisposed to oral-oropharyngeal cancer, but to a lesser extent than did tobacco chewing; smoking potentiated the carcinogenic effects of chewing in those who indulged in both habits.

1625 LEVELS OF SERUM CHOLESTEROL AMONG OFFSPRING OF PARENTS WHO DIED OF CANCER: A COMPARISON WITH CORONARY HEART DISEASE. (E.) Deutscher, S. (Dept. Prevent. Med., Dalhousie U., Halifax, Nova Scotia, Canada). *J Nat Cancer Inst* 46(2):217-224, 1971.

In an epidemiological study of the population of Teumseh, Michigan, the maternal mortality from cancer was shown to be high in cases where the levels of serum cholesterol in the offspring were low; conversely, maternal mortality was low where serum cholesterol levels in the offspring were high. The correlation was more striking among deceased mothers of younger offspring. Thus, for sons aged 30-49 yr with low serum cholesterol, 8.3% of the mothers had died of cancer, while for sons in the same age group with high serum cholesterol, 4% of the mothers had died of

cancer. For sons aged 50 yr or more with low and high serum cholesterol, mothers dying of cancer were 13% and 11%, resp. The high maternal cancer mortality associated with low serum cholesterol levels represented a reversal of the trend noted for maternal deaths from coronary heart disease, in which higher deaths were associated with high serum cholesterol among offspring. The results obtained for paternal cancer mortality contrasted with those obtained for maternal cancer deaths; a greater percentage of fathers died from cancer at an earlier age when their sons and daughters had relatively high serum cholesterol levels than fathers of offspring with low cholesterol levels. It was speculated that persons with low serum cholesterol contents possess other inheritable characteristics which they transmit to their offspring, and which are related to cancer development among younger women.

1626 PERIPHERAL MEASURABLE BRONCHOGENIC CARCINOMA: GROWTH RATE AND PERIOD OF RISK AFTER THERAPY. (E.) Weiss, W. (Hahnemann Med. Coll., Philadelphia, Pa.). *Amer Rev Resp Dis* 103(2):198-208, 1971.

The relationship between the growth rate of bronchogenic carcinomas and survival was investigated in 41 male lung cancer patients with solid tumors whose diameter could be measured on roentgen films. At the time of detection of the tumors 46% of the tumors measured 2.0-2.9 cm in diameter, and 11 measured 4.0-4.9 cm. Forty percent of the tumors were squamous cell carcinomas, 19% were undifferentiated carcinomas, 33% were adenocarcinomas, and 8% were mixed tumors. All but 2 of the squamous cell carcinomas and all but 1 of the undifferentiated carcinomas doubled in volume in less than 6 months, while 59% of the adenocarcinomas had doubling times longer than 6 months. There was no apparent correlation between survival of patients treated with radiation and doubling time of the tumors. When survival of patients treated by resection of rapidly growing tumors was plotted against doubling time from the time that the tumors were 2 cm in diameter, 2 populations could be separated. In one group 16 men died within a period of 52 months with rapidly growing tumors; in the other group, 7 patients had markedly longer survivals, some surviving at the termination of the study (10 yr), and 1 dying 113 months after his tumor had attained a diameter of 2 cm. For men with rapidly-growing cancers, there seemed to be a period of risk of about 50 months from the time the tumor reached 2 cm in diameter. For men with slowly-growing cancers a period of risk could not be satisfactorily extrapolated.

1627 PROLIFERATION KINETICS OF SARCOMA-180. (E.) Nishioka, B. (Kyoto Prefect. U. Sch. Med., Japan). *Gann* 61(6):563-568, 1970.

Cellular proliferation kinetics of sarcoma-180 in C3H mice has been studied both peripherally and centrally through ^3H -thymidine labeling. Six of 7 transplanted tumors grew continuously showing exponential gain by the 7th day after transplantation with the growth curve declining gradually and reaching a pla-

teau by the 12th day. Changes in the percentages of labeled mitotic figures for the tumors at 5, 8 and 12 days revealed essentially similar curves. The duration of the mitotic cycle varied from 13.5-14.5 hr, while the period of DNA synthesis ranged from 7.0 to 8.5 hr, the postsynthetic phase from 3.0 to 4.5 hr, and the postmitotic phase from 1.7 to 3.2 hr for all groups. Labeling indices varied from 43.8% for the 5-day-old tumor to 29.1% for the central portion of the 12-day-old tumor, showing a tendency toward gradual decline with development of the tumor. Mitotic indices ranged from 1.5% to 1.0% in the 5-day-old and 12-day-old tumor, resp., while the peripheral growth fraction was approximately 72.1% in all tumors. The present results appear to favor the concept that the slowing down of the growth rate may be explained on the basis of reduction of the growth fraction; however, increase in cell death may also be a contributing factor.

1628 CLINICAL STUDY AND TOPOGRAPHICAL DISTRIBUTION OF MALIGNANT TUMORS OF THE FACE AND NECK IN TUNISIA: SEVEN HUNDRED CASES FROM THE NATIONAL CANCER INSTITUTE OF TUNIS. (Fr.) Brugere, J. (Inst. Gustave Roussy, Villejuif, France) and A. Zaouche. *Bull Cancer* 57(3):345-354, 1970.

1629 AN EPIDEMIOLOGIC EVALUATION OF THE INCIDENCE AND MORTALITY OF MALIGNANT LYMPHOGRANULOMATOSIS IN THE YEARS 1961-1965. (Pol.) Gadomska, H. (Inst. Oncol., Warsaw, Poland) and Z. Karewicz. *Przegl Epidemiol* 24(4):511-516, 1970.

1630 TUMORS OF THE HEPATOBILIARY TRACT: MORTALITY IN CALABRIA WITH SPECIAL REFERENCE TO THE PROVINCES OF CATANZARO AND COSENZA. (It.) Grande, P. (Tumor Diagn. Treatment Ctr., Catanzaro, Italy). *Med Soc* 20(9):327-331, 1970.

1631 THE TUMOR REGISTRY OF QUEBEC: ANALYSIS OF THE ANNUAL REPORTS, 1964-1968. (Fr.) Pot R. (Tumor Registry of Quebec, Canada) and C. Auger. *Un Med Canada* 100(2):301-304, 1971.

1632 DEATH CERTIFICATION OF MALIGNANT MELANOMA: A PROBLEM IN EPIDEMIOLOGY. (E.) Carter, P. (Sch. Publ. Hlth. Commun. Med., U. Washington, Seattle) and J. A. H. Lee. *Amer J Epidemiol* 93(2):77-78, 1971.

1633 MALIGNANT NEOPLASIA OF THE SCALP AND TONSILS IN MOROCCO. (Ger.) Körbler, J. (Zagreb, Yugoslavia). *Oesterr Z Krebsforsch* 25(6):429-432, 1970.

1634 ON POSSIBLE CLINICAL EXAMINATIONS OF BIOLOGICAL ACTIVITY OF TUMORS OF THE PAROTID GLAND WITH RADIOISOTOPES. (Ger.) Agranat, V. Z. (P. A. Herzen Sci. Res. Inst. Oncol., Moscow, USSR) S. L. Dar'jalova and Je. A. Rabinovic. *Radiobiol Radiother* 11(6):649-653, 1970.

See also:

- * (Rev): 1281
- * (Chem): 1369
- * (Immun): 1531

MISCELLANEOUS

1635 ELECTRON PROBE ANALYSIS FOR IODINE IN HUMAN THYROID AND PARATHYROID GLANDS, NORMAL AND NEOPLASTIC. (E.) Banfield, W. G. (Nat'l. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), P. M. Grimley, W. G. Hammond, C. M. Taylor, B. DeFlorio and A. J. Tousimis. *J Nat Cancer Inst* 46(2):269-273, 1971.

Tissues from normal thyroid, normal parathyroid, thyroid adenomas, parathyroid adenomas, medullary carcinomas of the thyroid, and thyroid carcinomas were examined for iodine content using the electron probe X-ray microanalyzer. All normal thyroid glands and thyroid adenomas contained iodine; however, with 1 exception, none of the parathyroid glands, parathyroid adenomas, medullary carcinomas of the thyroid, or undifferentiated or follicular thyroid carcinomas contained iodine. In normal thyroid and thyroid adenomas, iodine was found in amounts exceeding 0.004% (the minimal limit of detectability) in the follicular colloid. Cells lining the follicles of thyroid and thyroid adenomas did not contain iodine. Iodine, where present, remained detectable in sections stained with hematoxylin and eosin.

1636 SUBRIBOSOMAL PARTICLES SEPARATED FROM LIVER AND HEPATOMA HOMOGENATES WITH A ZONAL ROTOR. (E.) Mullock, B. M. (Wolfson Bioanal. Ctr., W. Surrey, Guildford), R. H. Hinton, M. Dobrota, D. Broomberg and E. Reid. *Europ J Biochem* 18(4):485-495, 1971.

Subribosomal particles which had been labeled *in vivo* were isolated in quantity from rat liver and hepatoma homogenates by centrifugation in a zonal rotor, and the RNA content was analyzed by means of electrophoresis and base-ratio analysis. Subribosomal particles containing rapidly labeled RNA were separated at 47,000 rpm for 165 min from liver and transplanted hepatomas to give 3 or 4 fractions. The 40S region was free from contamination by ribonucleoprotein from other regions but showed heterogeneity in itself, the 60S and 80S regions were contaminated with material from neighboring regions and with ferritin. The 40S region contained rapidly labeled RNA which differed from that expected for 28S RNA, indicating the presence of non-ribosomal RNA. The hepatoma 40S region gave no evidence of heterogeneity, and the 60S region contained large amounts of ribonucleoprotein in the form of large ribosomal subunits. The differences between hepatoma and liver in the proportion and characteristics of the subribosomal particles may reflect differences between normal and tumor tissues in the control of protein synthesis which is governed by the supply of different components of polysomes.

1637 TARTRATE-RESISTANT ACID PHOSPHATASE ISOENZYME IN THE RETICULUM CELLS OF LEUKEMIC RETICULOENDOTHELIOSIS. (E.) Yam, L. T. (New England Med. Ctr. Hosp., Boston, Mass.), C. Y. Li and K. W. Lam. *New Eng J Med* 284(7):357-360, 1971.

Leukocyte acid phosphatase isoenzymes were studied in 6 normal subjects, 5 patients with chronic lym-

phocytic leukemia, 2 with generalized lymphosarcoma with neoplastic cells in the peripheral blood, and 3 with leukemic reticuloendotheliosis. Leukocyte suspensions were prepared from blood, centrifuged and subjected to electrophoresis. Normal subjects and patients with lymphosarcoma and chronic lymphocytic leukemia showed 4 isoenzyme bands, with isoenzyme 1 stronger than 2, 3 or 4 in normals, and isoenzyme 3 predominating in leukemia patients. Tartaric acid inhibited the activity of all 4 isoenzymes in these subjects. Five isoenzymes were seen in the leukemia reticuloendotheliosis patients, and the 5th was predominant. Fluoride and molybdate inhibited all 5 isoenzymes in these patients; tartaric acid inhibited isoenzymes 1-4 but not isoenzyme 5. In leukemic reticuloendotheliosis, the acid phosphatase in monocytes, eosinophils, neutrophils and lymphocytes was similar to the acid phosphatase in these cells in normal subjects. In all subjects, reticulum cells showed acid phosphatase activity; this activity was resistant to tartaric acid. In leukemic reticuloendotheliosis patients, isoenzyme number 5 was located almost exclusively in the reticulum cells; this enzyme may be useful as a marker enzyme for leukemic reticuloendotheliosis.

1638 MEASUREMENT OF THYROCALCITONIN-LIKE ACTIVITY IN URINE OF PATIENTS WITH MEDULLARY CARCINOMA. (E.) Voelkel, E. F. (Harvard Sch. Dent. Med., Boston, Mass.) and A. H. Tashjian, Jr. *J Clin Endocr* 32(1):102-109, 1971.

A method for concentrating hypocalcemic activity from the urine of 10 patients with medullary carcinoma of the thyroid gland by means of adsorption with powdered silica is described. The final concentrated eluate contained detectable amounts of hypocalcemic activity when the original urine was from patients with medullary carcinoma, but the final eluate from normal subjects had no detectable activity even when concentrated 100 times. The concentrated material gave log dose-response lines in the bioassay which were linear and parallel to the Medical Research Council Research Standards with values of 0.2 to 72 MRC mU/ml urine compared to the normal excretion of less than 0.2 MRC mU/ml. Acute rises in serum thyrocalcitonin followed infusions of both calcium and glucagon with a rise in urinary excretion of hypocalcemic activity in subsequent collection periods for patients with medullary carcinoma. The knowledge that a positive relationship exists between plasma and urine thyrocalcitonin levels should make it easier to perform metabolic clearance studies and perhaps utilize urine bioassays as diagnostic tools.

1639 EFFECT OF OLEIC AND LINOLEIC ACIDS ON THE MONODESATURATION *IN VITRO* OF STEARIC ACID BY THE LIVERS OF PATIENTS SUFFERING FROM MALIGNANT NEOPLASTIC DISEASES. (E.) Nakazawa, I. (Tohoku U. Sch. Med., Sendai, Japan), S. Yamagata and M. Uchiyama. *Tohoku J Exp Med* 102(3):283-288, 1970.

Abnormal metabolic regulation in the mono-desaturation of stearic acid in human livers of patients suffering from malignant neoplastic diseases was examined *in vitro* using biopsy homogenates. Mono-

desaturation of labeled stearic acid to oleic acid was recognized in 5 cases of non-malignant disease and in 6 cases of malignant neoplastic disease with values of mono-desaturation percentages ranging from 4.1 to 20.9 in the non-malignant cases and between 3.8 and 10.8 in the malignant neoplastic cases on the basis of desaturating activity per 50 mg protein of the enzyme preparation. Inhibitory effects of oleic acid and linoleic acid in the conversion of labeled stearic acid was observed in all non-malignant liver homogenates, but in malignant cases the inhibition was observed in only 1 of 3 cases with respect to oleic acid and in only 2 of 6 cases with respect to linoleic acid. Where inhibitory effects of both acids were examined, the inhibition percentage values with oleic acid were larger than with linoleic acid in non-malignant as well as malignant neoplastic cases. Abolition of the inhibitory effect should be examined with respect to other metabolic reactions, such as esterification of free fatty acids and phospholipid synthesis to clarify present findings.

1640 FLUORESCENCE CYTOPHOTOMETRIC FEULGEN-DNA MEASUREMENTS OF BENIGN AND MALIGNANT HUMAN TUMORS. (E.) Böhm, N. (Dept. Path. U. Freiburg, Germany), E. Sprenger and W. Sandritter. *Beitr Path* 142(2):210-220, 1971.

Benign and malignant (primary and secondary) human tumors were examined for DNA distribution patterns utilizing fluorescence Feulgen cytophotometry. Histograms of an adenoma of the prostate, cystadenoma of the ovary, fibromyoma of the uterus and spindle cell leiomyosarcoma of the uterus revealed DNA content to be diploid in character, whereas those obtained from malignant tumors revealed hyperdiploid, triploid and tetraploid, hypertetraploid, hexaploid and octoploid DNA ranges (adenocarcinoma of the endometrium, squamous carcinoma of the bronchus and clear cell renal carcinoma). Metastatic lesions revealed DNA content which ranged from hypertetraploid to hyperoctoploid peaks mainly with an anaplastic choriocarcinoma of the uterus showing DNA values up to 20-ploid. In general doubling peaks were much less prominent in benign lesions than in malignant conditions.

1641 RNA DIRECTED DNA SYNTHESIS: IDENTIFICATION IN L5178Y MOUSE LEUKEMIC CELLS AND DISTRIBUTION OF THE POLYMERASE IN A SYNCHRONIZED L5178Y CELL POPULATION. (E.) Bosmann, H. B. (U. Rochester Sch. Med. Dent., New York). *FEBS Letters* 13(2):121-123, 1971.

Characteristics of an RNA dependent DNA polymerase from L5178Y mouse leukemic cells and its activity during normal DNA synthesis were studied utilizing thymidine cell labeling. The enzyme showed lack of degradation by RNase and degradation by DNase, trichloroacetic acid insolubility, and alkali resistance and was dependent on Mg^{2+} and dATP, dCTP and dGTP. Yeast RNA was relatively ineffective as a template. The enzyme was active throughout the cell cycle with highest activity occurring at 9.5 hr post-mitosis in the early M period. The results indicate

that RNA dependent DNA polymerase is active throughout the cell cycle and apparently is present for formation transfer from RNA viruses or for gene amplification.

1642 PLASMA AND TUMOR CONTENT OF STEROIDS AND STEROID SULFATES IN TWO CASES OF ADRENOCORTICAL VIRILIZING CARCINOMA. (E.) Saez, J. M. (Hosp. Debrousse, Lyon, France), B. Loras, A. M. Morera and J. Bertrand. *J Steroid Biochem* 1(4):367, 1970.

The isolation and measurement of several C-19 and C-21 steroids in both unconjugated and sulfate form in 2 cases of adrenal virilizing tumors in children are reported including plasma concentrations in peripheral and adrenal veins by means of radioactive labeling and gas chromatography. Tumor tissue of case II quantitated by means of gas-liquid chromatography gave the following results: dehydroepiandrosterone 2.96 $\mu\text{g/g}$ tissue; sulfated derivative 7.1 $\mu\text{g/g}$ tissue; pregnenolone 0.95 $\mu\text{g/g}$ tissue; pregnenolone sulfate 3.12 $\mu\text{g/g}$ tissue. With a double isotope dilution technique, readings were similar. In the aldosterone fraction of both tumors, in the cortisone fraction of case I, and in the deoxycorticosterone fraction of case II, a constant $^3\text{H}/^{14}\text{C}$ ratio could not be obtained due possibly to low tumor content. Tumor tissue from case I revealed the presence of unconjugated androstenediol, corticosterone, 11-deoxycortisol and cortisol in addition to androstenediol sulfate, while tissue from case II was positive for androstenediol, corticosterone, 11-deoxycortisol and sulfated androstenediol. Peripheral plasma concentrations were generally elevated in both instances with increases in 5-en- 3β -ol steroids in case I and 11 β -hydroxyandrostenedione in case II. In patient II, for all steroids measured with the exception of unconjugated testosterone, the levels in adrenal vein plasma were 2-10 times higher than in peripheral plasma, indicating secretion of the steroids by the tumor. In both cases, significant quantities of testosterone sulfate were isolated, although the tumors did not secrete unconjugated testosterone.

1643 ADENOSINE METABOLISM IN PLASMA AND PLATELETS: IV. ELEVATED PLASMATIC ADENOSINE DEAMINASE ACTIVITY, IMPAIRED PLATELET ^{14}C -ADENOSINE INCORPORATION AND HEMOSTATIC DYSFUNCTION IN CHRONIC MYELOID LEUKEMIA. (E.) Pinkhas, J. (Tel-Aviv U. Med. Sch., Israel), J. J. Chivot, H. Michel and J. Caen. *Rev Eur Etud Clin Biol* 15(10):1108-1113, 1970.

Adenosine deaminase activity (ADA) in plasma from 12 patients with chronic myeloid leukemia was determined by ^{14}C -inosine formation from ^{14}C -adenosine in plasma. ADA was elevated in 11 of 13 examined patients; in 1 patient, ^{14}C -inosine activity was at 46.1 nM/min, as compared to 19.4 nM/min for a normal control; ADA levels were generally elevated by a factor of 2-3 in leukemia patients. The effect of leukemic plasma on platelet ^{14}C -adenosine incorporation was observed in 5 patients; ^{14}C -adenosine incorporation in platelets incubated with leukemic plasma was generally reduced by a factor of 1.5-2. No relation

ship was found between elevated ADA and peripheral WBC and RBC counts, differential counts, and hemoglobin determination. ADP consumption was increased in 8 and normal in 3 patients with leukemia. Most patients also had decreased serum aggregating activity, decreased platelet acid phosphatase availability and normal platelet factor 4. Platelet aggregation studies performed with leukemic platelets in their own plasma showed that the aggregation induced by collagen, ADP and epinephrine were generally abnormal. Primary hemostasis in chronic myeloid leukemia seems to depend on an interaction of plasmatic factors such as ADP and adenosine degradation and intracellular factors such as platelet adenosine incorporation and release of platelet nucleotides.

544 LYMOPROLIFERATIVE DISEASES OF FOWL: ALTERATION IN LACTATE DEHYDROGENASE ISOZYMES ASSOCIATED WITH LYMPHOBLASTIC LEUKEMIA (JM-V). (E.) Adams, M. L. (Dept. Anim. Dis., U. Connecticut, Storrs), A. J. Kenyon, N. D. Jones, F. Schmidt and S. N. Kim. *J Nat Cancer Inst* 61(1):43-48, 1971.

Elevated serum lactate dehydrogenase isozyme levels associated with JM-V (a highly lethal strain of neurotropic lymphoproliferative disease of domestic fowl) lymphoblastic leukemia were investigated in many-old sex-linked, Barred Rock-Rhode Island Red crossbred cockerels by photodensitometry. Serum levels of lactate dehydrogenase and isocitrate dehydrogenase increased abruptly between 4 and 5 days post-inoculation to 21,400-33,700 U and 9,520 U of lactate dehydrogenase and isocitrate dehydrogenase, resp., on the 6th post-inoculation day compared to controls with 1,240-1,630 U for lactate dehydrogenase and 1,110 U for isocitrate dehydrogenase, while serum glutamate-oxalacetate transferase levels ranged from 380-810 U compared to 305-390 U in controls. At 6 days post-inoculation, spleen weights ranged from 110-346 mg whereas spleen controls ranged from 2-41 mg; liver weights ranged from 2.2-4.2 g in infected fowl as opposed to a range of 1.3-3.1 g in controls; bursa weights remained unchanged. Peripheral smears revealed numerous lymphocytes and large lymphoblasts in various stages of mitosis during the period of rapid increase in lactate dehydrogenase and isocitrate dehydrogenase. Isozyme distribution during increased lactate dehydrogenase is similar to that in lymphoid tissue as represented by the bursa, suggesting the lymphoblast as the main source of this alteration in enzyme levels.

545 LYSOSOMAL ENZYME ACTIVITY IN LIVER TISSUE, KIDNEY TISSUE, AND TUMOR TISSUE FROM PATIENTS WITH RENAL CARCINOMA. (E.) Schersten, T. Wahlgrenska Hosp., Göteborg, Sweden), L. Wahlgren and B. Jilderos. *Cancer* 27(2):278-283, 1971.

Lysosomal enzyme activity was investigated in liver tissue, kidney tissue, and kidney tumor tissue in patients with renal carcinoma. Total activities of acid phosphatase, aryl sulfatase, cathepsin and glucuronidase in livers from renal carcinoma patients were increased compared to these activities

in patients without renal carcinoma. In controls, liver acid phosphatase activity totaled 14.75 μ moles P_i /mg protein/min and cathepsin totaled 4.70 μ moles tyrosine split/mg/min; in renal carcinoma patients, values for liver acid phosphatase and cathepsin were, resp., 18.63 and 5.96 μ moles/mg/min. Cathepsin activity was found to be higher in patients with comparatively large renal tumors. The activities of lysosomal enzymes in kidney tissues from renal carcinoma patients were similar to those activities in livers of controls; however, aryl sulfate activity was higher in renal carcinoma patients' kidney tissue than in control livers. Enzyme activities in renal carcinoma tissue were lower than in liver and in non-malignant kidney tissue; acid phosphatase in the peripheral part of renal tumors was 5.47 μ moles P_i /mg/min. Ratios between total and free enzyme activity were higher in the areas than in the central parts of the tumors, the differences between central and peripheral free/total ratios being 1.2 for acid phosphatase and 1.4 for aryl sulfatase and cathepsin. High activities of lysosomal enzymes tended to be found in tumors of patients having high total enzyme activities in liver tissue. Lysosomal enzymes may be released from tumor tissue to be taken up by other tissues where they continue to be active.

1646 VARIATION OF DIHYDROFOLATE REDUCTASE ACTIVITY DURING *IN VITRO* AND *IN VIVO* GROWTH OF SUBLINES OF L1210 LYMPHOMA. (E.) Hillcoat, B. L. (Dept. Biochem., McMaster U., Hamilton, Ontario, Canada). *J Nat Cancer Inst* 46(1):75-80, 1971.

The increased activity of the enzyme dihydrofolate reductase (DHFR) in methylcholanthrene-induced lymphomas was studied by establishing three cloned strains of L1210 lymphoma cells in the DBA strain of mouse. The doubling time of LS2, LM1, and LM4 clonal lines was initially 16 hr *in vitro* and increased to 19 hr 3 months later, growing logarithmically for 2-2½ days. *In vivo* ascites cells grew logarithmically after a lag of 1 day with a doubling time of 24 hr for 2 days followed by a slower increase. Clones LS2 and LM1 caused death of all treated animals by day 12 while animals carrying LM4 cells survived and showed a decrease in cell count after day 10. LS2 cells contained 40 chromosomes including a subtelocentric marker similar to that found in the parent line; LM4 and LM1 were hypoploid with 36 chromosomes each, with the former possessing the subtelocentric marker. Fifty percent growth inhibition of LS2, LM1, and LM4 cells occurred at 2.5×10^{-9} , 1×10^{-8} , 3.5×10^{-8} M methotrexate, resp. Maximum DHFR activities of the 3 cell lines were similar *in vitro* and *in vivo* with the LM4 cells containing 5-6 times the amount of enzyme of the LS2 cells and 9 times that of LM1 cells. The specific activity of DHFR of LM4 cells *in vivo* was 10 times that of LS2 and LM1, but only five times *in vitro*. Cell count, protein concentration and enzyme activity were closely related; however, specific activity tended to change less than enzyme activity per 10^7 cells *in vitro*, indicating a rate of loss of DHFR comparable to the bulk of cellular protein. The significant differences of

the three clonal lines reflect the heterogeneity of the parent L1210 cells.

- 1647 ISOLATION OF A TUMOR FACTOR RESPONSIBLE FOR ANGIOGENESIS. (E.) Folkman, J. (Child. Hosp. Med. Ctr., Boston, Mass.), E. Merler, C. Abernathy, and G. Williams. *J Exp Med* 133(2):275-288, 1971.

A tumor angiogenesis factor (TAF) mitogenic to capillary endothelial cells was isolated from various different tumor tissues and shown in experiments with rats to promote vascular proliferation *in vivo*. Isolation of the TAF was achieved by high-speed centrifugation of tumor tissue homogenates and fractionation in column chromatography. Walker 256 ascites tumors, B-16 mouse melanomas, human neuroblastomas, Wilms' tumors and hepatoblastomas all demonstrated TAF; human neuroblastomas showed the greatest ability to promote vascular proliferation. TAF was found to be composed of RNA and proteins, and it was suggested that blockage of the TAF factor may arrest solid tumors in the early stages of growth.

- 1648 STIMULATION OF LIVER DNA SYNTHESIS BY A FACTOR FROM ASCITES TUMOR 6C3HED. (E.) Yarbro, J. W. (U. Kentucky Med. Ctr., Lexington). *Int J Cancer* 7(1):176-181, 1971.

Partial isolation and characterization of a factor from 6C3HED mouse ascites tumor capable of stimulating liver DNA synthesis in non-tumor bearing animals is reported. Incorporation of label into the liver DNA of young C3H mice was a function of time in which a plateau was reached within 2 hr for labeled orthophosphate and within 30 min for labeled thymidine. After inoculation of the ascites tumor, a gradual increase in the rate of label incorporation was seen compared to controls. Maximum stimulation of DNA synthesis was seen at 100 hr after injection of 0.005 ml ascites fluid. DNase and RNase did not abolish liver-stimulating activity but pronase markedly diminished this activity. The factor responsible for the liver-stimulating activity requires further purification and characterization.

- 1649 COLLAGENOLYTIC ACTIVITY IN THE SIMPLE SOLID CARCINOMA OF THE BREAST, RELATED TO DNA CONTENT. (Ger.) Keiditsch, E. (St. Hosp. Munich, Germany) and L. Strauch. *Verhandl Deutsch Ges Path* 54:438-442, 1970.

The increase in collagenase activity in the area of a solid mammary carcinoma was investigated to discover whether the increase was related to the increased number of tumor cells or whether the carcinoma cells themselves generated more collagenase. The tissues of the center of the carcinoma, the periphery, and the carcinoma free zone were examined for collagenase activity, DNA content and nitrogen content. The distribution of enzyme activity showed the enzyme to be increased in the periphery and decreased in the central core of the carcinoma, with lowest activity in the healthy tissue. The increase in collagenase activity was related to the DNA content,

indicating a higher production of enzyme by the tumor cells in this area. The increased collagenase activity in the periphery of the carcinoma appeared to be the result of an increase in the formation or deposition of the enzyme in the cancer cells, perhaps as an invasive factor in the growth of mammary carcinoma.

- 1650 STUDIES ON THE PEROXIDASE OF EXPERIMENTAL CHLOROMA. (Jap.) Tsuchimochi, T. (Showa U. Sch. Med., Tokyo, Japan). *Acta Haemat Jap* 33(4):388-401, 1970.

An experimental chloroma began to grow noticeably 1 wk after transplantation in rats and showed a high level of peroxidase activity at that time. Peroxidase activity was most conspicuous in the mitochondrial and lysosomal fractions of chloroma cells. Isolated peroxidase was thought to be bound with porphyrin and nucleic acid from its absorption spectrum. The bound nucleic acid was RNA, was readily isolated from the peroxidase, was similar to sRNA, and had a sedimentation coefficient of 5S on column chromatographic analysis. The porphyrin bound to peroxidase was protoporphyrin and had no influence on the peroxidase activity itself. The green pigmentation consisted mainly of peroxidase which had the characteristics of myeloperoxidase. It was thought that the porphyrin might have been bound to the peroxidase protein at the site of a vinyl bond.

- 1651 STUDY ON THE PROPOSED ROLE OF PHOSPHOLIPIDS IN TUMOR CELL MEMBRANE. (E.) Selkirk, J. K. (McArdle Lab. Cancer Res., U. Wisconsin, Madison). J. C. Elwood and H. P. Morris. *Cancer Res* 31(1):27-31, 1971.

The phospholipids in plasma membranes from slowly and rapidly growing solid hepatomas and from normal liver cells were compared; the structural alterations, degree of membrane fatty acid unsaturation, and amount of calcium and magnesium in the membranes were determined. The 2 hepatomas studied were the Morris 3924A tumor, an anaplastic, rapidly growing neoplasm, and the Reuber H-35 hepatoma, which has a relatively slow transplantation time. The Reuber tumor and normal liver cells had the same percentages of the individual plasma membrane phospholipids. The Morris tumor plasma membrane, however, contained plasmalogen (diphosphatidyl) glycerol amounting to 7.2% of total phosphorus, while the Reuber tumor and liver cells had no choline; the Morris tumor cell membrane 21.2% of total phosphorus was found in sphingomyelin, while percentage of sphingomyelin phosphorus for Reuber tumor and normal cell membranes were 8.3 and 9.1%, resp. The Morris tumor cell membrane contained 53% unsaturated lipid fatty acids, while percentages of unsaturated fatty acids from liver cells and Reuber tumors were 42 and 35%, resp. Both tumors showed increased membrane-bound calcium compared to liver cells, with Morris tumor membrane containing more calcium (88 µg/g dry wt) than the Reuber tumor membrane (233 µg/g). Liver cell membranes contained more magnesium

(89.5 $\mu\text{g/g}$) than either the Morris (33.6 $\mu\text{g/g}$) or the Reuber (69.6 $\mu\text{g.g}$) tumor cell membranes.

1652 COMPARISON OF THE MITOCHONDRIAL MEMBRANE PROTEINS IN RAT LIVER AND HEPATOMAS. (E.)

Chang, L. O. (U. Virginia Sch. Med., Charlottesville), C. A. Schnaitman and H. P. Morris. *Cancer Res* 31(2): 108-113, 1971.

Mitochondrial membrane proteins isolated from the liver mitochondria of normal rats and rats bearing hepatomas showed similar major protein bands on polyacrylamide gel electrophoresis. Mitochondrial membrane proteins were also isolated from well-differentiated, poorly differentiated, and undifferentiated hepatomas (H-35, 9098, H35-tc1, H35-tc2 and 3924-A). Gel patterns from tumor mitochondrial membranes were significantly different from those of livers from normal rats and from tumor-bearing rats. One major protein band observed in the membranes from normal liver was lacking or greatly reduced in all of the hepatoma membrane samples. Membranes isolated from a well-differentiated hepatoma (H-35) had an additional major band which was present in lesser amounts in other hepatoma membranes and which was absent or exiguous in the normal liver membranes.

1653 THE HORMONE-SYNTHESIZING TROPHOBLASTIC CELL IN VITRO: A MODEL FOR CANCER RESEARCH AND PLACENTAL HORMONE SYNTHESIS. (E.)

Pattillo, R. A. (Med. Coll. Wisconsin, Milwaukee), G. O. Gey, E. Delfs, W. Y. Huang, L. Hause, J. Garancis, M. Knoth, J. Amatruda, J. Bertino, H. G. Friesen and R. F. Mattingly. *Ann NY Acad Sci* 172(10):288-298, 1971.

A human choriocarcinoma was established as a cell line *in vitro* by serial transplantation in hamster cheek pouches, and the properties of the trophoblastic cells of the tumor were examined. Cells contained many desmosomes, active Golgi apparatus, and normal mitochondria. Human chorionic gonadotropin was produced by trophoblasts of the carcinoma in amounts similar to those produced by normal uterine cells; 1,000-5,000 IU of gonadotropin from the trophoblast cultures failed to stimulate an ovarian or uterine response, but 1 IU of follicle-stimulating hormone added to the gonadotropin produced hyperstimulation of ovarian activity and uterine hypertrophy. The trophoblast cell line produced small amounts of human placental lactogen, which correlated with the low levels of this hormone produced by patients with choriocarcinoma. Analysis of steroid biosynthesis in the tumor cells demonstrated the presence of the placental enzyme 3- β -ol dehydrogenase, in addition to progesterone and androstene. Methotrexate inhibited trophoblast growth; incubation of cells with a 10^{-5} M concentration of methotrexate inhibited the uptake of ^3H -uridine by cells in DNA synthesis by 100%; a concentration of 10^{-9} M of methotrexate produced no inhibition of label incorporation. The trophoblast cell line's karyotype remained stable through 150 passages, the modal number remaining 78-86. Malignant choriocarcinoma cells were found to have a transmembrane electrical potential of 35-50 mv, the lower value at pH 7 and the higher value at pH 8. The role of the sialomucin cell coat in producing the charged surfaces remains unclear.

1654 FLUOROGENIC AMINES IN THE C-CELLS THYROID TUMOURS OF MAN. (E.)

Beskid, M. (Postgrad. Med. Sch., Warsaw, Poland) and R. Lorenc. *Acta Histochem* 38(1):74-81, 1970.

Biopsy specimens from 12 human adenomas and 2 hyalinic medullary carcinomas revealed autofluorescence in collagen fibers under fluorescence microscopy. Unfixed sections treated with formaldehyde gas showed a yellowish fluorescence; the fluorescence was stronger in some cells than in others. Unfixed sections treated *in vitro* with dihydroxyphenylalanine showed no increase in yellow fluorescence. Substances isolated from the thyroid adenoma tissue produced a hypocalcemic effect when injected into rats. The observed yellow fluorescence was attributed to the presence of fluorogenic amines in the C-cell thyroid adenomas and carcinomas.

1655 LIPID METABOLISM IN CULTURED CELLS: GROWTH OF TUMOR CELLS DEFICIENT IN ESSENTIAL FATTY ACIDS. (E.)

Bailey, J. M. (George Washington U. Sch. Med., Washington, D.C.) and L. M. Dunbar. *Cancer Res* 31(2):91-97, 1971.

Growth of Ehrlich ascites carcinoma and sarcoma 180 were studied in normal CF₁ mice and CF₁ mice with pronounced essential fatty acid deficiency through periodic assay of the fatty acid composition in whole blood. Mice fed a fat-free diet grew more slowly than controls during the first 5 wk at which time they ceased growing, while control mice continued to gain weight for a further 4-6 wk. The sharpest decline in blood linoleic acid occurred during the first month in the deprived animals with a drop in blood lipids from 17.5% to less than 5% of the total fatty acid; at 6 months blood lipids decreased to 0.5% or less than 1/30 of the normal amount. Growth of tumors from cells harvested from Ehrlich ascites carcinoma showed a similar pattern in normal and deficient mice with a somewhat longer lag phase following inoculation. Similarly, cells harvested from a sarcoma 180 showed a somewhat longer lag period after inoculation into the deficient mice, but mean generation times measured over the entire growth curve were not significantly different. The total lipid content of the Ehrlich ascites tumor of the deficient mice (0.76 ± 0.13 mg lipid/ 10^7 cells) was not significantly different from that of normal cells (0.67 ± 0.12 mg/ 10^7 cells) despite decreases in linoleic acid and arachidonic acid due to simultaneous increases in palmitoleic acid, oleic acid, and eicosatrienoic acid. Increase in dividing time occurred in the initial stages of growth when both Ehrlich ascites and normal sarcoma 180 cells were transplanted into deficient mice, but growth rate returned to normal after the first 24-48 hr. This fact and the apparently normal transplantation characteristics of the deficient cells in both normal and deficient hosts suggests that the deficient environment did not represent any major metabolic stress.

1656 ECTOPIC PRODUCTION OF HUMAN CHORIONIC SOMATOMAMMOTROPIN BY NONTROPHOBLASTIC CANCERS. (E.)

Weintraub, B. D. (Natl. Inst. Arthri-

tis Metab. Dis., Natl. Inst. Hlth., Bethesda, Md.) and S. W. Rosen. *J Clin Endocr* 32(1):94-101, 1971.

Eleven of 128 patients with confirmed malignancies in sites other than trophoblastic or gonadal sites were found to have human chorionic somatomammotropin (HCS) in their plasma; case material in which HCS was detected included plasma from patients with lung carcinoma, hepatoma, lymphoma or leukemia, and pheochromocytoma. Unconcentrated plasma was examined in all cases; where HCS was not detected, the plasma was concentrated by affinity chromatography for re-examination. Of 80 subjects without malignancy, none had HCS in direct assay; none of 18 normal subjects whose sera were tested after concentration by affinity chromatography had HCS. Nine lung cancer patients showed HCS only in the concentrated serum examinations. Of 13 patients with untreated trophoblastic tumors, 8 had detectable HCS, and of 9 patients with treated trophoblastic tumors, one had detectable HCS. Untreated trophoblastic tumor patients had concentrations of HCS which were generally higher than those in patients with nontrophoblastic tumors. Unconcentrated serum of trophoblastic tumor patients showed HCS concentrations with maxima of 180 and 75 ng/ml, while maximum HCS concentrations in unconcentrated sera of patients with nontrophoblastic tumors were 14 and 9 ng/ml. Tumor extracts from 4 patients with undifferentiated large cell carcinomas of the lung and from 2 patients with choriocarcinoma contained HCS, whereas nonmalignant tissues from the same patients had no detectable HCS; in these patients, tumor and plasma HCS concentrations showed significant correlation. HCS production in these 4 patients was thought to be ectopic. The ectopic production of HCS suggests there is a link between ectopic hormones and ectopic embryonic proteins, and may indicate the presence of neoplasm.

1657 STIMULATION OF DNA SYNTHESIS *IN VITRO* IN MOUSE THYMIC CELLS BY BONE MARROW PREPARATION. (E.) Knyszynski, A. (Weizmann Inst. Sci., Rehovot, Israel) and M. Burger. *Blood* 37(2):231-239, 1971.

A factor present in mouse bone marrow preparations (BMP) which stimulates DNA-synthesis in mouse thymic cells *in vitro*, was compared with mouse kidney and spleen cell preparations. Incubation of thymic cells with the kidney cell preparation failed to stimulate DNA synthesis, and incubation with the spleen cell preparation reduced DNA synthesis from normal values by approximately 30%. BMP increased DNA synthesis in thymic cells by 41%, but human serum 19S alpha-2 globulin did not increase thymic DNA synthesis. BMP did not increase DNA synthesis in mouse mesenteric lymph node cells or in bone marrow cells. Protein synthesis in mouse thymic cells was stimulated only 24% by BMP; BMP stimulation of DNA occurred in the absence of protein synthesis (when blocked by puromycin) as well as in cells synthesizing protein. The bone marrow factor increased thymic DNA synthesis by 26% in mice with thymic leukemia as compared to a 46% increase in normals. The bone marrow factor stimulated thymic cell DNA synthesis only half as much in mice given 300 r of whole-body irradiation as in unirradiated mice. Puri-

fied bone marrow factor was resistant to heating at 100° even at low or high levels of acidity; however the factor was more sensitive to heat denaturation if it was in an impure state. Treatment with RNase, I pronase and carboxypeptidase did not affect the stimulatory activity of the bone marrow factor.

1658 STUDIES ON THE ORIGIN OF PROTEINS IN THE NUCLEOLI OF MOUSE ASCITES TUMOR CELLS: A TEST FOR PROTEIN TRANSFER TO THE NUCLEOLI. (E.) Kawashima, K. (Natl. Cancer Ctr. Res. Inst., Tokyo, Japan), M. Izawa and S. Sato. *Biochim Biophys Acta* 232(1):192-206, 1971.

A transplanted mouse ascites tumor cell line was used in pulse-chase experiments of amino acids to investigate the transfer of protein molecules to the cell nucleolus from other cellular structures. Cessation of amino acid incorporation by the nucleolus after the pulse was achieved by administration of a 7500-fold excess of unlabeled amino acid and/or of 100-200 µg/ml cycloheximide to cells in culture. Radioactive-labeled proteins were found to increase by 70-100% in nucleoli during pulse-chase experiments; the increase in nucleolar proteins appeared to be the expense of small but significant decreases in radioactive protein in the cytoplasmic 25,000 x g supernatant fraction. In addition to the nucleoli, the 25,000 x g cytoplasmic sediment which may contain mitochondria and the extranucleolar nuclear fraction which consists of chromatin and nuclear scaffolds were found to receive proteins through transfer during the chase. The decline in radioactive-labeled proteins in the 25,000 x g cytoplasmic supernatant fraction during the chase appeared to be the result of a decrease in the 105,000 x g sediment fraction. A smaller increase was found in labeled proteins in the 105,000 x g supernatant fraction. The nucleolar 105,000 x g supernatant fraction and the nucleolar 105,000 x g sediment fraction appeared to be receiving sites for proteins synthesized elsewhere. Protein transfer to the nucleolus was diminished by lowering the temperature of the pulse-chase process; addition of 2,4-dinitrophenol to the medium diminished the amount of protein transferred to the nucleolus by 60%. Actinomycin D also suppressed the transfer of protein to the nucleolus. Apparently, incorporation of amino acids into the nucleoli in the living animal depends at least in part on the uptake of protein molecules produced on the outside of the nucleolus, probably in the cytoplasmic polyribosomes.

1659 ON THE REGULATION OF THE SYNTHESIS OF RIBOSOMAL PROTEINS IN L-CELLS. (E.) Craig, N. C. (Div. Biol. Sci., U. Maryland, Baltimore). *Molec Biol* 55(1):129-134, 1971.

The effect of low doses of actinomycin D on the synthesis of ribosomal proteins and ribosomal RNA was studied by isotopic labeling and electrophoresis in mouse L-cell fibroblasts. The cells were labeled with ¹⁴C-amino acids first and then with ³H-amino acids in the presence of actinomycin D (0.12 µg/20 ml). In the soluble protein fraction the ³H/¹⁴C ratio remained unchanged during the 11 hr of re-

covery even though the specific activity decreased by about 45% due to dilution with unlabeled newly synthesized protein. Relative ribosomal-soluble $^3\text{H}/^{14}\text{C}$ ratio from the cells after 11 hr of recovery was significantly less than 1.00, implying that the production of effective ribosomal protein has been specifically inhibited in comparison to synthesis of soluble protein. These results imply a co-ordinated regulation of the production of ribosomal RNA and ribosomal protein.

1660 ISOTOPE DILUTION DETERMINATIONS AND OTHER STUDIES OF CYTIDINE DIPHOSPHATE CHOLINE, CYTIDINE DIPHOSPHATE ETHANOLAMINE, DEOXYCYTIDINE DIPHOSPHATE CHOLINE, AND DEOXYCYTIDINE DIPHOSPHATE ETHANOLAMINE IN LIVER AND LIVER TUMORS. (E.) Schneider, W. C. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *J Nat Cancer Inst* 46(2):435-441, 1971.

The choline and ethanolamine content of normal and regenerating rat liver and of hepatomas in Sprague-Dawley rats was studied by means of isotope dilution determinations. Concentrations of deoxycytidine diphosphate-choline and deoxycytidine diphosphate-ethanolamine was much greater in the Novikoff hepatoma than in normal liver with decreases in choline and increases in ethanolamine 24 hr after partial hepatectomy. The concentration of cytidine diphosphate-choline was about the same in normal and Novikoff hepatomas and doubled 12 hr after hepatectomy in hepatoma 5123, while cytidine diphosphate-ethanolamine concentrations were greater in hepatoma 5123 and in regenerating liver at both 12 and 24 hr after partial hepatectomy compared to normal liver. Homogenates of the Novikoff hepatoma incubated with labeled deoxycytidine diphosphate ethanolamine showed significant incorporation into DNA; suppression of this activity resulted from the addition of P-ethanolamine cytidyl transferase compared to enhanced incorporation by cells treated with labeled deoxycytidine diphosphate. No evidence for the conversion of cytidine diphosphate-choline to deoxycytidine diphosphate-choline or for direct incorporation of deoxycytidine diphosphate-ethanolamine into the DNA of the Novikoff hepatoma was found; no satisfactory explanation can be given for the increased levels of deoxycytidine diphosphate-choline and ethanolamine in hepatomas and regenerating liver.

1661 HYBRID CELLS IN SOLID TUMORS. (E) Janzen, H. W. (Surg. Med. Res. Inst., U. Alberta, Edmonton, Canada), P. A. Millman and O. G. Thurston. *Cancer* 27(2):455-459, 1971.

In vitro hybridization between cells of murine lines Sarcoma-180 (Foley) and L-5178Y lymphoblast was studied in 131 C3H mice over a 21-day period through observation of growth characteristics and karyotype analyses. Chromosome analysis of 100 cells of Sarcoma-180 in isolated culture showed 92 low ploidy and 8 high ploidy cells with the chromosome numbers for the stemline cells ranging from 80-90, whereas 100 cells of L-5178Y consisted of 70 low and 30 high ploidy cells with the number for the low ploidy cells ranging from 38-43 and for the high ploidy from 76-86. Chromosome analysis of 200

apparently intact cells of mixed *in vitro* cultures showed 9 cells to be hybrids with a complete or near complete set of chromosomes from each parent line. *In vivo* tumor growth analysis revealed Sarcoma-180 (Foley) grew progressively as a solid tumor in the thigh muscle reaching an average diameter of 2.6 cm in 28 mice with no evidence of metastasis 21 days after inoculation; the L-5178Y tumor appeared as a palpable mass within 5 days after inoculation and reached a maximum average diameter of 0.9 cm in 25 mice on the 8th post-inoculation day after which it regressed completely with no evidence of metastasis on day 21; the mixed lymphoblast tumor reached a maximum average diameter of 1.2 cm in 32 animals on the 8th day followed by regression which remained as a small focus at the site of inoculation but produced no metastatic lesion. Chromosome analysis of both pure tumors showed no change in karyotype as a result of passage through the host mice, whereas hybrid cells appeared with the mixed tumor. The low frequency of hybrid cells in the mixed tumor makes it unlikely that the intermediate behavior of these tumors is determined by such cells.

1662 ELECTRON MICROSCOPIC STUDY OF BRONCHOGENIC SQUAMOUS EPITHELIAL CARCINOMA CELLS. (Ger.) Zimmer, S. (Cytodiag. Central Lab., Grimma, Germany) and M. Kühnert. *Z Erkrank Atmungsorg* 132(3):351-354, 1970.

Electron microscopic studies were conducted in histologically confirmed bronchogenic squamous epithelial carcinoma with the object of finding possible structural specificity. Some of the general changes in malignancy as seen by the electron microscope were: loss of ciliary differentiation, loss of polarity, a change from metaplasia to anaplasia, transformation to squamous epithelia, and coagulation necrosis. Nuclear changes were invagination, marginal condensation of the chromatin, and infiltration. Changes seen in the cytoplasm and its organelles were enlargement of intercellular vacuoles, broad desmosomes, peripheral condensation of fibrils, disturbances in the internal structure of the mitochondria, thickening of the endoplasmic reticulum, dilatation, cleft formation, cisterns, sequestration, and increased lysosomes.

1663 NUCLEAR POCKETS ASSOCIATED WITH THE NUCLEOLUS IN NORMAL AND NEOPLASTIC CELLS. (E.) Burns, E. R. (U. Arkansas Med. Ctr., Little Rock) B. L. Soloff, C. Hanna and D. F. Buxton. *Cancer Res* 31(2):159-165, 1971.

Nuclear pockets appearing as simple invaginations of the nuclear envelope filled with cytoplasm were found in cells prepared from Ehrlich ascites tumor, chick embryo lens, human amelanotic malignant melanoma of the ciliary process, and human corneal epithelium from Fuchs' dystrophy. Nuclear pockets, although seen in all cell preparations, were most common in malignant melanoma cells. Many of the pockets extended toward the nucleoli or were otherwise associated with them. Nuclei with multiple pockets or with branching pockets were rare. Nuclear pockets may

function to increase nuclear-cytoplasmic interaction by increasing their contact surface area.

- 1664 AMYLOID-LIKE DEPOSITS IN LUNG CANCER AND BRONCHIAL ADENOMA. (Ger.) Kozlowski, H. (Med. Acad. Gdansk, Poland), M. Hrabowska and R. Polonski. *Arch Geschwulstforsch* 36(4):370-384, 1970.

Morphological analysis of pulmonary carcinoma and bronchial adenoma tissues was performed with particular attention to amyloid-like deposits; the material for analysis comprised 129 cases of lung cancer and 21 cases of bronchial adenoma and was collected either from biopsies or autopsy specimens. Among the lung carcinomas, 4 cases of oat-cell carcinoma showed hyaline masses which were positive to Congo Red and appeared both in the primary lesion and in the metastases. The cellular structure of the tumors included solid uniform epithelial conglomerations. Diffuse stroma and few blood vessels were seen, and fibrocytes and collagen fibers were observed in the area of the vascular bed. The nuclei still contained some chromatin and the nuclear bodies were sometimes seen faintly. Septum-like structures gave the carcinoma tissue an organoid appearance. Round, oval and spindle-shaped cells of varying size were seen in the mesh-like spaces. Rosette-shaped structures were found mostly in the periphery. Trabecular, tubular, and muff-like structures are described. Among the bronchial adenomas, 2 cases showed amyloid deposits with infiltration in the affected area and metastases in the regional lymph nodes. Glassy aggregates were seen in the stroma; amyloid deposits were seen in internal organs only in one case of undifferentiated lung cancer. The stimulating factors in the construction of amyloid-like substances in oat-cell carcinoma and in carcinoid bronchial adenoma are probably biologically active hormones produced by these tumors.

- 1665 EARLY HISTOGENESIS OF TRANSPLANTED MOUSE MAMMARY GLANDS: II. WITHIN 96 HOURS FOLLOWING ISOGRAFTING. (E) Chew, E. C. (Dept. Anat. U. Western Ontario, London, Canada) and K. Hoshino. *Z Anat Entwicklungsgesch* 132(4):318-324, 1970.

Female mice were given ^3H -thymidine i.p. in 4 injections of 50 μg ; 3 hr later mammary duct segments were excised and implanted into recipient females and the distribution of the label was observed 24, 48, 72 and 96 hr after transplantation. Twenty-four and 48 hr after transplantation, many labeled and non-labeled epithelial cells were seen scattered in the adipose tissues at the transplantation sites, indicating dissociation of the transplanted mammary duct segments. By 72 hr the scattered labeled cells had formed aggregates which often contained non-labeled epithelial cells. Heavily-labeled cells undergoing mitosis were often found in these aggregates. By 96 hr after transplantation, many mammary ducts had multilayered epithelia. Only after 72 hr did the basement membrane appear to be complete with regenerating mammary ducts in advanced stages; how-

ever, by 96 hr all stages of regeneration of transplanted mammary tissue were seen. Each graft ultimately developed into 1 mammary gland only.

- 1666 MALIGNANT CELLS IN THE BLOOD OF EYE PATIENTS. (E.) Stanford, G. B. (U. Utah Med. Sch., Salt Lake City) and A. B. Reese. *Trans Amer Acad Ophthalmol Otolaryngol* 75(1):102-109, 1971.

Blood samples from 31 patients with intraocular tumors were passed through filters to detect malignant cells borne in the blood. The filters contained 400,000 holes/cm², and the holes measured 5 μ in diameter. Some patients had received no treatment, and some had undergone enucleation; ocular tumors in the patient sample included malignant melanoma and retinoblastoma. No malignant cells were found in the blood of untreated patients. Of the 18 patients undergoing enucleation for retinoblastoma, there were 3 positive blood samples; all 3 eyes proved to have choroidal invasion by the retinoblastoma. None of the malignant melanoma patients treated by enucleation showed malignant cells in their blood; but 1 malignant melanoma patient undergoing photocoagulation had a positive blood sample. Retinoblastoma cells in the blood were stained with 3er alanffy's acridine orange stain. The presence of malignant cells in the blood is not necessarily relevant for the prediction of the development or location of metastases; for malignant cells can pass to distant sites by routes other than the circulating blood.

- 1667 SUBCELLULAR FRACTIONATION OF MOUSE MYELOMA CELLS. (E.) Choi, Y. S. (Dept. Pediat., Minnesota, Minneapolis), P.M. Knopf and E. S. Lenné. *Biochemistry* 10(4):659-667, 1971.

A method is described for studying precursor-product relationships in subcellular components of a BALB/c mouse myeloma cell line by means of sucrose density gradient centrifugation and choline and leucine labeling. Repeated centrifugations revealed fraction I, rough membranes (RM), to be the principal constituent with fraction II, a mixture of RM, smooth membranes (SM) and free polyribosomes; fraction III had a variety of SM and some free monoribosomes, and fraction IV consisted of free proteins and membrane. Leucine-labeled cells revealed 80% of the light chain in fractions containing membranes, 95% of which were rough membranes of fractions I and II. The light chain of fraction II was kinetically different from that observed in fraction I. While the fractions obtained were heterogeneous, there was sufficient enrichment of rough membranes in fraction I and smooth membranes in fraction III to be useful for distinguishing kinetically and chemically the differentiating properties of the intracellular light chains.

- 1668 LIGHT AND ELECTRON MICROSCOPY OF LOW AND HIGH MALIGNANCY SUBLINES OF A RAT TUMOR. (E.) Ratcliffe, N. A. (Dept. Zool., U. Leicester, England), A. E. Williams and H. Smith. *J Nat Cancer Inst* 46(2):243-252, 1971.

Ascites and solid abdominal and s.c. tumors of high and low malignancy cell lines in the rat differed structurally, but showed no specific cellular structures associated with degree of malignancy. Electron microscopic examination of ascites tumors showed mitochondria concentrated in the Golgi region; these mitochondria had unusual buds involving both mitochondrial membranes and the cristae. Buds were never observed free in cytoplasm, but remained attached to the mitochondria. The mitochondria in solid abdominal tumors were generally larger than those in ascites tumors; solid abdominal tumors also had buds. The mitochondria of the s.c. solid tumors were similar to those of solid and ascites tumors. The minor differences observed between tumor cells of different malignancy were probably attributable to differing metabolic environments or to changes in cell surface charge. The mitochondrial buds were not thought to be associated with malignancy.

1669 ULTRASTRUCTURAL STUDY OF HUMAN PARATHYROID ADENOMA AND THE OCCURRENCE OF ABNORMAL CILIA IN THE ADENOMA CELLS. (E.) Polyzonis, M. B. (Theagenion Cancer Inst., Tessaaloniki, Greece). *Path Europ* 5(4):454-469, 1970.

Although the number of cilia found in normal parathyroid tissue cells by electron microscopy did not exceed 2 cilia/cell, the number of cilia in parathyroid adenoma tissue cells often numbered 4/cell. Both normal and adenomatous parathyroids were composed primarily of chief cells, but the normal cells had few ribosomes while the adenoma cells had many. In the adenoma cells, cilia were found lying singly or in groups within pericilliary vacuoles; some cilia were found lying in the intercellular spaces between cell membranes; in normal parathyroid tissue, cilia were never found lying free in intercellular spaces. Naked cilia were seen in the cytoplasm in some adenoma cells, but not in normal parathyroid cells. The association of cilia with immature cells may suggest that the overabundance of cilia in parathyroid adenoma cells is an expression of the immaturity of the tumor cells.

1670 SURFACE PROPERTIES OF HUMAN MELANOMA CELLS. (E.) Lapis, K. (U. Med. Sch., Budapest, Hungary) and M. Radnot. *Amer J. Ophthalmol* 71(3):740-750, 1971.

The surface properties of cells taken from 2 human ocular melanomas were examined by electron microscopy; ultrathin sections were stained with Luft's ruthenium red stain. Both tumors were composed of spindle-A cells and were thought to be benign. Cells showed a fairly even layer of stain on their surfaces, the layer's thickness varying from 14-20 nm. No nonspecific deposits of ruthenium red were seen. The stain did not enter the cells, but it did react with the limiting membrane of pinocytic vesicles which were either about to be detached from the plasmalemma or which had just been detached, but were still close to the cell membrane. Higher magnification revealed that deposits of stain sometimes accumulated where the parallel cell membranes approached each other, possibly representing the cell bridges observed with conventional electron microscope techniques. No stain was

seen on the membranes of degenerating cells; however, degenerating necrobiotic cells stained with ruthenium red usually showed a higher degree of electron-density than surrounding intact cells. The binding of the stain to cell components apparently results in increased electron density, for the limiting membranes of necrobiotic cells appeared to become permeable to the stain.

1671 TERATOMAS OBTAINED THROUGH EXTRAUTERINE GROWTH OF SEVEN-DAY MOUSE EMBRYOS. (E.) Damjanov, I. (Med. Fac. U. Zagreb, Yugoslavia), D. Solter, M. Belicza and N. Skreb. *J Nat Cancer Inst* 46(3):471-480, 1971.

Seven-day mouse embryos, transplanted under the kidney capsules of adult mice, produced teratomas which were either histologically well-differentiated and regarded as benign, or poorly differentiated and regarded as malignant. Small portions of 6 large (10-15 g in wt) and 4 small (1-3 g in wt) tumors were transplanted under the femoral fascia of syngeneic mice; 13 of 27 large tumor grafts grew in hosts, while none of the small tumor grafts took. Tumors obtained by retransplantation were microscopically similar to primary tumors arising after egg cylinder implantation. Large, well-differentiated teratomas contained many kinds of differentiated tissues stemming from all 3 germinal layers, including glia, ependyma, squamous epithelium, and bone. Differentiated tumors had the ultrastructural appearance of adult tissue, and included well-formed intracellular structures. The cytoplasm of poorly differentiated cells was typical of that of embryonal carcinoma; it showed abundant ribosomes, but lacked other organelles except for well-developed Golgi bodies, a few mitochondria and occasional rough endoplasmic reticulum material. Intermixed with these typical undifferentiated cells were other undifferentiated cells displaying some cytoplasmic specialization such as myofibrils, secretory granules and distorted microvilli. That the undifferentiated cells retained an embryonal appearance was thought to account for the continuous malignant growth of these embryonally derived teratomas.

1672 THE OCCURRENCE OF "NUCLEAR BODIES" IN BENIGN AND MALIGNANT HUMAN NEOPLASMS. (Ger.) Schremmer, C. N. (Robert Rossle Clin., German Acad. Sci., Berlin). *Arch Geschwulstforsch* 36(4):360-369, 1970.

The intranuclear structure of nuclear bodies found in benign and malignant human tumors was investigated by electron microscopy. The evaluation of the 143 tumors which consisted of epithelial and mesenchymal tumors was made on the basis of similar histological diagnosis. Nuclear bodies were found in 32 groups out of the 34 selected for their histological similarity, but these bodies were also seen in the stromal cells. No particular relationship could be found between the tumor type and the specific structure of the nuclear body. It was possible to conclude from the results that a common capacity for higher differentiation could be attributed to the nuclear bodies, although only in a very few tumors was there an overwhelming number of mature nu-

clear bodies. It was also concluded that the nuclear bodies are not likely to be of viral origin, but that they may be related to increased hormonal activity or to the introduction of toxic material.

- 1673 THE CONTROL OF GROWTH OF MAMMALIAN CELLS IN AXENIC CULTURE: THE ROLE OF CONFORMATION OF GROWTH REGULATORY PROTEINS. (E.) Tritsch, G. L. (Roswell Park Mem. Inst., New York St. Dept. Hlth., Buffalo), G. Grahl-Nielsen and J. A. Bell. *J Med* 1(2):90-100, 1970.

The effects of reversible urea denaturation, disulfide bond reduction and reoxidation, and intramolecular cross-linking on the growth regulatory activity of various calf serum proteins were investigated using a cell line derived from a small bowel carcinoma in the hamster. Reduction of disulfide bonds, accomplished by adding mercaptoethanol to the cell preparations, reduced the growth regulatory activity of the fetal calf serum in the hamster tumor cell culture. At levels of more than 0.1 mg calf serum protein/ml of culture, mercaptoethanol-treated cells showed densities decreasing to zero. Exposure of the proteins to 8 ml of urea followed by a removal of the urea resulted in enhancement of growth stimulatory activity in excess of the levels encountered in untreated calf serum. Reduction of disulfide bonds by mercaptoethanol treatment in the presence of urea practically abolished growth stimulatory activity. Intramolecular cross-linking of calf serum proteins with 1,5-difluoro-2,4-dinitrobenzene also produced materials practically devoid of growth regulatory activity. Conformation of serum proteins is apparently an important factor in determining their growth regulatory activity.

- 1674 STIMULATION OF CELL PROLIFERATION IN MOUSE KIDNEY BY ISOPROTERENOL. (E.) Malamud, D. (Massachusetts Gen. Hosp., Boston) and R. A. Malt. *Lab Invest* 24(2):140-143, 1971.

The effect of isoproterenol (IPR) injections on cell proliferation was investigated in the kidneys of mice given 0.025-11 mg of IPR i.p.; nucleic acid synthesis was followed by ^3H -thymidine and ^3H -uridine incorporation. Renal DNA synthesis reached its maximum 34 hr after a single injection of 9 mg of IPR; this maximum represented a 6-fold increase in DNA synthetic activity over that in kidneys not given IPR, but was smaller than the response seen in the parotid gland. DNA synthetic activity declined when doses of IPR exceeded 9 mg. Incorporation of ^3H -uridine into total renal RNA was depressed about 40% for 8 hr after injection of IPR, and then increased moderately above control values. IPR injection also produced a transient decline in ^{14}C -labeled phenylalanine incorporation into renal protein. Cellular hypertrophy, as measured by the ratio of RNA to DNA, was not elevated in kidney tissue after IPR injection as it was in the parotid gland. DNA synthesis was increased by combination doses of IPR and theophylline more than it was increased by IPR alone, suggesting that cyclic 3', 5'-adenosine monophosphate was implicated in the initiation of cell proliferation by IPR.

- 1675 GROWTH OF MULTICELL SPHEROIDS IN TISSUE CULTURE AS A MODEL OF NODULAR CARCINOMA. (E.) Sutherland, R. M. (Ontario Cancer Treatment Res. Fdn., London, Canada), J. A. McCredie and W. J. Inch. *J Nat Cancer Inst* 46(1):113-120, 1971.

Chinese hamster V79 lung cells in suspension culture were grown to study the effects of nutrition and oxygenation on growth as well as the effect of drugs on radiation through autoradiography and photomicrographs. Small aggregates of 5-10 cells formed during the initial hours in culture and accounted for the rapid increase in mean volume of the spheroids which increased directly with the initial cell number and with the concentration of fetal calf serum. Subsequent growth which occurred by cell division to form multicell spheroids was exponential for 4 days, decreased and then approached a horizontal asymptote on the 9th day. Cells were similar until spheroid reached a diameter of about 200 μ ; then pyknotic cells appeared centrally and centrinodular necrosis developed in larger spheroids. Three distinct zones were noted in continuous labeling with ^3H -thymidine; mitotic cells were uniformly distributed until the spheroid reached a diameter of 150 μ when the mitotic index began to decrease from 3.1% to reach 0.7% at 370 μ . Electron micrographs showed cellular communication to be similar to that of organized tissue with tight, intermediate and desmosome junctions visible. The multicell spheroid has several advantages as an *in vitro* tumor model since its shape facilitates the use of mathematical equations for calculating the number of cells and diffusion of metabolites.

- 1676 MORPHOGENIC AND MITOGENIC EFFECTS OF PROLACTIN ON RAT MAMMARY GLAND *IN VITRO*. (E.) Dilley, W. G. (Dept. Zool., U. California, Berkeley). *Endocrinology* 88(2):514-517, 1971.

The effects of insulin (25 U/mg) and prolactin (28 U/mg) on mitotic activity was investigated in rat mammary gland cultures of 0-5 days. After 1 day in culture, no alveolar activity was observed in cultures of mammary cells treated with insulin or with prolactin. However, after 5 days insulin-treated cultures had attained alveolar grade 0.9, and cultures treated with both insulin and prolactin had attained alveolar grades 2.5-3.0. On day 1, cultures treated with insulin only showed 1.0-1.3% mitotic figures, and cultures treated with insulin and prolactin showed 2.0-2.7% mitotic figures. On day 5, insulin-treated cultures had 0.2-0.3% mitotic figures, and cultures treated with insulin and prolactin showed 1.1-1.2% mitotic figures. Pattern of DNA synthesis in cells cultured with insulin alone were not markedly altered by the addition of prolactin. In epithelial cells cultured with insulin and prolactin, DNA synthesis showed a log-dose response to increasing doses of prolactin. Results were reliable only for epithelial mammary gland cells and not for fibroblasts or for total mammary gland cells. Prolactin appeared to be mitogenic for epithelial cells.

- 1677 VARIATION OF THE TRANSMEMBRANE POTENTIAL LEVEL AS A BASIC MECHANISM OF MITOSIS CONTROL. (E.) Cone, C. E., Jr. (Langley Res. Ctr. Hampton, Va.). *Oncology* 24(6):438-470, 1970.

correlation between mitotic activity and the transmembrane electrical potential (E_m) of cells is well established; mitotic quiescence is generally associated with high E_m values, mitotic activity with low E_m values. The correlation is especially striking in tumor cells; the E_m of myosarcoma cells was found to be -10 mV, as compared to E_m value of -90 mV for adjacent normal cells. Changes in the cell membrane accompanying malignant transformation and adaptation of living cells to culture conditions may also be causally associated with the observed changes in cell membrane E_m in malignant cells. On the basis of the observed correlation between E_m and mitosis, a model was proposed according to which intracellular ionic conditions associated with changing E_m values regulates DNA synthesis in the cell and other preconditions for mitosis. The model's plausibility was supported by findings on record that imposition of intracellular ionic conditions approximating those at an E_m level of -70 mV (equivalent to the E_m of a nondividing nerve cell) reversibly blocked DNA synthesis and mitosis *in vitro*. The model postulated sets forth a system of feedback circuits operating in the cell to link those mechanisms in the cell membrane which control E_m with features of cellular metabolism and with environmental osmotic factors, including surface contact with other cells and the presence of hormones in the vicinity of the cell. (53 references)

1678 EFFECTS OF ACTINOMYCIN D AND PUROMYCIN ON DIFFERENT PHASES OF THE LIFE CYCLE OF PHA-STIMULATED LYMPHOCYTES *IN VITRO*. (E.) Stolzmann, W. M. (Med. Acad. Poznan, Poland). *Bull Acad Pol Sci* 18(10):663-668, 1970.

The sensitivity of different phases of the cell cycle to actinomycin D and puromycin was studied in cultures of phytohemagglutinin (PHA)-stimulated peripheral lymphocytes in media with methotrexate and adenosine. Actinomycin D (0.1 and 1.0 μ g/ml of culture) added 9-12 hr before the start of DNA synthesis with 14 C-thymidine caused a decrease of the number of labeled cells to approximately 50%; when added 16 hr prior to the start of DNA synthesis this decrease did not occur. Similar results occurred with puromycin. Actinomycin D and puromycin added to cultures at the time of reversal of DNA synthesis did not affect the number of labeled cells during the last 8 hr of the S period. However, after 2 hr of incubation, the grain count/cell was reduced to 50% of the control value. In a third group of cells in which reversal of the inhibitory effects of methotrexate was followed by addition of actinomycin D, suppression of cell division occurred during the subsequent 24 hr. The effect of actinomycin D was more pronounced during the S period. Results suggest during euchromatin replication. Results suggest that at least 2 actinomycin D- and puromycin-sensitive mechanisms control the DNA synthesis in these stimulated lymphocytes.

1679 ELECTRON MICROSCOPIC AND CHROMATOGRAPHIC STUDY ON MALIGNANT TUMOR CELLS INVADING FAT CELLS. (Ger.) Wessel, W. (Path. Inst. U. Bonn, Germany). *Verhandl Deutsch Ges Path* 54:454-458, 1970.

The invasion of tumor cells into the surrounding fat tissue was investigated in 10 medullary solid mam-

mary carcinomas. The infiltration into the fatty tissue was marked by collagen formation. The electron microscopic demonstration of tumor invasion into the fat alveoli showed the peripheral reticulum to consist of numerous irregularly formed processes with hyaloplasm. The appearance of the tumor cells suggested high surface motility compared to normal cells which are limited by the basal membranes. Two invasion factors appeared to be the high motility of the tumor cell membranes which inhibited the formation of basal membranes and thus were in contact with the reticular network, and tumor cell phagocytosis of the fat cells. The latter was not seen in all cases. The fatty globules were seen to be broken up into smaller particles in the cytoplasm of the tumor cell and was shown to be unchanged by chromatographic techniques.

1680 LYSOSOMAL CHANGES AND ENHANCED METASTATIC GROWTH: AN EXPERIMENTAL STUDY OF THE EFFECTS OF SOME NON-IONIC SURFACTANTS. (E.) Carter, R. L. (Roy. Cancer Hosp., London, England), M. S. C. Birbeck and J. A. Stock. *Int J Cancer* 7(1): 34-49, 1971.

The effects of treatment with each of 4 non-ionic surfactants on tumor development and metastasis were investigated in female golden hamsters implanted with metastasizing lymphoma or non-metastasizing lymphoma in the flank. About 2-15 days after tumor implantation, hamsters were given i.p. injections of either Triton W-1339 detergent (1,000 mg/kg), poly 15 (1,000 mg/kg), poly 30 (1,500 mg/kg) or macrocyclon (850 mg/kg). Treatment with the detergents enlarged the size of hepatocytic lysosomes; normal lysosomes, which measured 0.2 μ , were enlarged approximately 10-fold. The detergents produced a moderate fall in tumor wt (untreated control hamsters' tumors had mean wt of 12 g, while mean wt for tumors of hamsters given Triton and macrocyclon were 7.2 and 6.8 g, resp.). However, detergent-treated animals showed increased metastatic spread compared to controls. While metastases involving the axillary nodes, anterior mediastinum, liver and mesenteric nodes occurred in many hamsters both treated and untreated, treated animals also showed metastatic involvement in the posterior mediastinum, lungs, spleen or ovaries. Metastatic growth in control hamsters was focal, while in detergent-treated animals metastatic growth was diffuse. Both treated and untreated hamsters showed high liver/body wt ratios, high liver acid phosphatase activity, and liver lysosomal damage; however, these changes were more pronounced in treated hamsters than in controls. The mechanism of increased metastatic spread in detergent-treated hamsters may be due to the lysosomal damage caused by the detergents in lysosome-rich organs such as the liver. No metastasis was caused by detergents with the non-metastasizing lymphoma.

1681 SIGNIFICANCE OF THE SIZE DISTRIBUTION OF BLOODBORNE METASTASES. (E.) Douglas, J. R. S. (Roy. Newcastle Hosp., New South Wales, Australia). *Cancer* 27(2):379-390, 1971.

A model based on the notion that metastasis is a random process in which events may occur from the

moment of initial transformation of the primary focus of tissue into malignant tissue has been constructed to provide a means for explaining the biological behavior of metastasizing neoplasms. In postmortem examination of organs, no indication of abrupt augmentation of the rate of metastasis formation was observed as may be expected if the primary neoplasm gained in activity on proceeding from one stage of anatomical spread to another. Where diameters of the metastatic spheres were greater than the thickness of the sections, marked deviation from a straight line was noted on plotted measurements. Evidence of a decline in metastases formation to almost complete suppression was noted in 3 cases treated by tumor excision and 1 by therapeutic radiation. Typical plots appeared to result in a rectilinear curve for early metastases with subsequent deviation and trend toward formation of fewer metastases.

- 1682 STUDIES ON THE MECHANISMS OF INVASION IN CANCER: II. *IN VIVO* EFFECTS OF A FACTOR CHEMOTACTIC FOR CANCER CELLS. (E.) Ozaki, T. (Kumamoto U. Med. Sch., Japan), K. Yoshida, K. Ushijima and H. Hayashi. *Int J Cancer* 7(1):93-100, 1971.

Although tumor-free rats failed to respond to injections of a chemotactic substance for cancer cells isolated from tumor tissue, rats previously inoculated with 2.5×10^5 rat ascites hepatoma cells/ml showed extravascular emigration of circulating tumor cells following an injection of 50 or 70 μ g of cancer cell chemotactic substance. Emigration of tumor cells was observed within 24 hr of injection, and by 72 hr postinjection, the number of emigrated cancer cells had markedly increased at the injection site, the proliferation being especially intense in the subcutaneous tissue. By 11 days postinjection, cancer cells had invaded the muscles under the injection sites to form a metastatic secondary tumor. No emigration of polymorphonuclear leukocytes was seen. Injection of the chemotactic tumor cell factor did not increase vascular permeability; however, injection of permeability factors isolated from tumor tissues, and of histamine or bradykinin failed to produce tumor-cell emigration. Injection of a factor chemotactic for polymorphonuclear leukocytes produced pronounced leukocyte emigration from the venules followed by infiltration of the cells throughout the skin tissue, but did not cause cancer cell migration. These results suggest that malignant invasion may involve a chemotactic factor.

- 1683 SEQUENCE OF EVENTS IN EXPERIMENTAL METASTASES OF WALKER 256 TUMOR: LIGHT, IMMUNO-FLUORESCENT, AND ELECTRON MICROSCOPIC OBSERVATIONS. (E.) Jones, D. S. (Dept. Path., U. Western Ontario, London, Canada), A. C. Wallace and E. E. Fraser. *J Nat Cancer Inst* 46(3):493-504, 1971.

Young adult rats were given tail-vein injections of Walker 256 tumor cells and killed 2 min-72 hr later, at which time the spread and disposition of the tumor cells were observed. Staining of sections of tissue was with hematoxylin-eosin, Lendrum's stain for fibrin, and immunofluorescent staining for fibrin. At

2 min post-inoculation, light and electron microscopic examination detected tumor cells in groups of 1-6 in pulmonary arteries and capillaries and in small arterioles; all cells were intravascular, and partially or entirely surrounded by a pink meshwork which stained as fibrin with Lendrum's stain. Platelets could be seen in this meshwork. Immunofluorescent stains gave strong reactions for fibrin. From 1-49 hr after inoculation, the number of tumor cells was seen to decline steadily; however, after 49 hr post-inoculation, tumor cells increased rapidly, and by 72 hr there were 3 times the number of cells seen at 48 hr. Numbers of platelets associated with the tumor cells declined with time from inoculation; fibrin also decreased. The endothelial lining was breached by tumor cells, and by 24-48 hr the cells were clearly perivascular and lying in apposition to the connective tissue.

- 1684 ANNULATE LAMELLAE IN CULTURED HUMAN NEUROBLASTOMA CELLS. (E.) Goldstein, M. N. (Washington U. Sch. Med., St. Louis, Mo.). *Cancer Res* 31(3):209-213, 1971.

Distinctive annulate lamellae were observed in cultures of neuroblasts prepared from tissue explants from human neuroblastomas. Tissue samples were taken from tumor metastases in the lymph nodes of 3 children under 5-yr-old and from an abdominal tumor from a fourth child. Cells from the cultures were prepared for electron microscopy after 10-160 days in culture. The immature neuroblasts contained scant cytoplasm, rough endoplasmic reticulum and many free ribosomes. Nuclear pores were seen in sections cut tangentially to the nuclear surface, and arrays of annuli were seen in the cytoplasm of about 5% of the neuroblasts, and their morphology corresponded to that of the nuclear pores. Annuli were associated with lamellae, a series of undulating membranes which were continuous with the annuli. The annulate lamellae may be the result of a relaxation of the mechanism responsible for new nuclear membrane synthesis.

- 1685 NEPHROBLASTOMA: A CHROMOSOMAL STUDY. (Fr.) Rousseau, M. F. (Paris, France), M. Laurent and C. Nezelof. *Ann Anat Path* 15(4):399-414, 1970.

In a chromosome analysis of 3 cases of nephroblastoma in human infants, the numerical anomalies were examined by means of a histogram of the distribution of mitoses as a function of their chromosome number and by the calculation of the mean chromosomal population of aneuploid mitoses; karyotype structural anomalies were studied, and supplementary chromosomes were classified. From the study of short term cultures, 334 mitoses were grouped and analyzed. The karyotype study of these cases showed either a diploidy with a slight tendency to polyploidy, or a aneuploidy with a homogeneous distribution about the

mode of 53 chromosomes. Structural anomalies were rare and no particular chromosome feature could be singled out. The chromosomal results of the short term cultures after 7, 13 and 22 days of culture led to the conclusion that there was no predominant selective effect. The results confirm reports found in the literature that a tumor type is not characterized by a common variant, and the karyotypes of the same tumor type are not generally identical; anormal karyotype can be found in a cell with a neoplastic character.

- 1686 ADDITIONAL EVIDENCE FOR CHROMOSOME ABNORMALITIES IN THE ERYTHROID PRECURSORS IN ACUTE LEUKAEMIA. (E.) Krogh Jensen, M. (U. Hosp. Copenhagen, Denmark) and S. A. Killmann. *Acta Med Scand* 189(1-2):97-100, 1971.

Karyotype studies were performed on bone marrow aspirates from 5 leukemia patients to detect chromosome abnormalities in these cells. The patients included 4 males and 1 female with myeloblastic leukemia, acute erythroleukemia, and promyelocytic leukemia. Two patients had hyperdiploid cell lines, 1 had a hypodiploid line, and 2 had pseudodiploid cell lines. In 1 instance, a minute acentric fragment was observed. The percentage of erythroid metaphases in leukemic marrow was found to be markedly higher than the percentage in marrow of normal subjects. From 16-62% of the mitotic figures in the bone marrow aspirates from the leukemia patients were erythroid, while the percentages of normal metaphases ranged from 0-22%. Chromosome abnormalities apparently are not confined to blastic cells in acute myeloid leukemia, but are also to be found in erythroid precursor cells. It was suggested on the basis of these findings that acute myeloid leukemia is a general disease of the hemopoietic system rather than a disease of the granulocytic cell line only.

- 1687 MULTIPLE CELL ORIGIN OF HEREDITARY NEUROFIBROMAS. (E.) Fialkow, P. J. (Dept. Med., U. Washington, Seattle), R. W. Sagebiel, S. M. Gartler and D. L. Rimoim. *New Eng J Med* 284(6):298-300, 1971.

Tumors and overlying skin from 2 Negro women with a total of 14 hereditary neurofibromas were examined to determine whether the tissues contained both A and B types of glucose-6-phosphate dehydrogenase. In females carrying both the A and B genes at the X-linked glucose-6-phosphate dehydrogenase locus, single cells express the activity of only 1 or the other gene. Therefore, it was thought that neoplasms arising from a single cell should exhibit only type A or B enzymes; the detection of both enzymes would indicate that the neoplasm had a multiple cell origin. Electrophoresis showed that both the A and B enzymes were present in each of the 14 tumors and in all specimens of overlying skin. Contamination of the tumor and overlying skin tissues with normal tissue was ruled out, and it appeared that the finding of the double enzyme phenotype in these subjects was a reliable indication of a multiple cell origin for the hereditary neurofibroma. The initial tumorigenic event associated with the development of neurofibroma may affect a few cells

which subsequently alter adjacent cells, or it may affect large numbers of cells simultaneously.

- 1688 MACROGLOBULINEMIA OF WALDENSTRÖM AND THE CHROMOSOMAL MORPHOLOGY. (E.) Goh, K. O. (Sch. Med. Dent., U. Rochester, N. Y.) and S. N. Swisher. *Amer J Med Sci* 260:237-244, 1970.

Peripheral leukocyte cultures and bone marrow preparations from patients with Waldenström's macroglobulinemia were subjected to cytogenetic examination. Karyotypes from 3 patients showed that 43% of metaphases contained an abnormally large chromosome, larger by 9-33% than the largest chromosome in the complement. The large chromosome was found to replace either the 1, 2 or 3 chromosome in group A. Large chromosomes were also found in 40% of metaphases from leukocytes of normal persons cultured with plasma from patients with Waldenström's macroglobulinemia. Only 10% of metaphases from normal control cultures showed the large chromosome. The abnormally large chromosome may have resulted from the different effects of colchicine on the cells of the Waldenström's macroglobulinemia patients. Colchicine exposure, in turn, may have resulted in one of the normal A chromosomes being coated with a large molecular-wt protein.

- 1689 GONADOBLASTOMA IN A PHENOTYPIC FEMALE WITH 45,X/47,YYY MOSAICISM. (E.) Sune, M. V. (Inst. Natural Sci., Fed. U. Rio Grande do Sul, Porto Alegre, Brazil), J. V. Centeno and F. M. Salzano. *J Med Genet* 7(4):410-412, 1970.

A case report of gonadoblastoma, a rare ovarian dysgenetic tumor, in a woman having a karyotypic picture previously unrecorded in connection with this condition is presented. The left ovary of the subject, a 21-yr old woman, was composed of cords of large round cells with vacuolated cytoplasm, the general aspect of which was similar to dysgerminoma. Other components of the affected ovary included cells with small oval nuclei showing calcified irregular concretions and fibrous stromas with nests of Leydig-like cells. Chromosome counts of peripheral leukocytes showed modal chromosome numbers of 45 and 47; and karyotype analysis of cells having these chromosome numbers showed a mosaicism of the 45,X/47,YYY type, which is unique in gonadoblastoma patients.

- 1690 45,X,G-,Ph¹ + CELL LINE IN BONE-MARROW AND BLOOD OF A CML AFFECTED MALE. (E.) Serra, A. (Catholic U. Sch. Med., Rome, Italy), S. Sargentini, C. Patrono, A. Ferrara and V. Laghi. *Ann Genet* 13(4):239-243, 1970.

Cytogenetic studies were performed on bone marrow and peripheral blood cells of a male patient with chronic myelogenous leukemia in whom bone marrow cells were found to contain the Ph¹ chromosome and to lack 1 of the G group chromosomes. In this case, chronic myelogenous leukemia was diagnosed on the basis of physical symptoms, hyperplastic bone marrow, and prevalence of myelocytes. Cytogenetic studies showed 45 chromosomes in both the bone mar-

row and blood cells and only 4 G group chromosomes in the blood cells and in 45% of the bone marrow cells. Ph¹ chromosome could be demonstrated clearly in 86 cell preparations from bone marrow, and peripheral blood cells showed a similar karyotypic pattern. It was speculated that the missing chromosome might be the Y, but this could not be ascertained.

- 1691 DNA REPLICATION PATTERNS IN CHROMOSOMES OF SEVERAL TRANSPLANTABLE ASCITES HEPATOMAS OF THE RAT. (E.) Sasaki, M. (Fac. Sci. Hokkaido U., Sapporo, Japan). *J Nat Cancer Inst* 46(1):25-35, 1971.

DNA replication patterns of transplantable ascites tumor cells in seven aneuploid strains of rats were investigated by means of short-term *in vitro* incubation with tritiated thymidine autoradiography. Labeled interphase cells ranged from 30-96%; the increase was proportional to incubation time, and a similar pattern was noted in metaphase cells with the exception of AH-13 and AH-13 and AH-41c strains in which the relation was inconsistent. In 7 of 11 cells analyzed in AH-130 1 telocentric element at the 847th generation was relatively late replicating. In 70% of the cells at least 1 or 2 elements of some of the largest telocentric members resembled the largest telocentric pair of the normal karyotype, and generally in early replicators 1-3 elements in the small metacentric group and 1-4 elements in the telocentric group were unlabeled in about 40-60% of the cells. In AH-41c, the tumor was characterized by the presence of large metacentric and medium-sized metacentric markers and a small telocentric marker corresponding in size and shape to the Y chromosome. AH-7974 karyotype was characterized by 2 minute dotlike elements and several abnormal submetacentric markers with Y-like elements in all 10 cells studied; AH-414 had 3 distinctive markers including a large metacentric, a minute, and a medium-sized subtelocentric with 2 prominent secondary constrictions on its long arm, whereas the karyotype of AH-272 had a large metacentric, subtelocentric and a medium-sized metacentric with both tumors showing relatively late or early segmental patterns. Replicatory features of chromosomes in transplantable ascites hepatomas are different from normal ones and the abnormal patterns may in some way be related to the drastic numerical and structural changes of chromosomes in the tumors.

- 1692 CYTOLOGICAL AND CYTOGENETICAL STUDIES ON BRAIN TUMORS: II. HYPERDIPLOIDY, A RARE EVENT IN HUMAN PRIMARY MENINGIOMAS. (E.) Zankl, H. (Max Planck Inst. Psychiat., Munich, Germany), H. Singer, K. D. Zang, H. Büscher and W. Kofler. *Humangenetik* 11(3):253-257, 1971.

The chromosomal findings among 70 human meningiomas were cytogenetically investigated through biopsy of brain tissue. The great majority of meningiomas showed an increasing hypodiploidy beginning with the loss of a G-group chromosome. Two tumors with a modal chromosome number of 53 (50-54) showed similar histological appearance representing a special

type of fibromatous meningioma in which an excess of D chromosomes was constant. The loss of G-group chromosomes could not be established in these tumors. In 1 meningioma, a true C-trisomy seemed to be present with the metacentric extra chromosome showing a marked secondary constriction at the proximal part of its long arm and another at its distal part. Findings in these 70 meningiomas indicated that the preferred chromosomal deviation consisted in the loss of a G-group chromosome with or without subsequent loss of further chromosomes.

- 1693 CHROMOSOMAL ANALYSIS OF LYMPHOBLASTOID CELL LINES AFTER HETEROSEXUAL COCULTIVATION WITH BONE MARROW FIBROBLASTS. (E.) Benyesh-Melnick, M. (Baylor Coll. Med., Houston, Tex.), M. Macek, E. H. Seidel and V. Mackova. *J Nat Cancer Inst* 46(2):369-382, 1971.

Chromosomal studies were carried out on lymphoblastoid cells from peripheral blood leucocytes and bone marrow of 10 female patients, 3 with acute leukemia and 7 with infectious mononucleosis; the cells were maintained in cocultivation with diploid human bone marrow fibroblasts from males. Karyotype studies of the leukemia and mononucleosis cell lines showed them to consist of 3 groups according to karyotype characteristic. One group showed a conventional 46,XX karyotype and included only infectious mononucleosis cell lines. Other groups showed marker chromosomes with a submedian centromere, a pseudodiploid clone, trisomy C, and polysomy C. T cell cultures were studied over 20-174 serial passages; the sex of the cell lines was found to have remained female. This suggested that the fibroblasts in which the lymphoblastoid cells were maintained had a feeder layer function, and were not transformed by an agent in the lymphoblastoid lines. Heteroploidy developed only in cells from patients with mononucleosis.

- 1694 REGULATION OF PHENOTYPIC EXPRESSION IN CROWN-GALL TERATOMA TISSUES OF TOBACCO. (E.) Meins, F., Jr. (Rockefeller U., New York, N.Y.). *Develop Biol* 24(2):287-300, 1971.

The physiological basis for stability of the teratoma phenotype in tobacco crown-gall tumors through developmental variants derived from cloned teratoma cells and phenocopies of the variant forms through chemical treatment of teratoma tissues in culture is described. Two phenovariants of cloned teratoma tissues were isolated as highly localized outgrowths with distinct morphology at the edge of the parent teratoma tissues and were propagated for 8 yr without reversion to the parent phenotype. Phenovariant A grew as a flattened glistening white sphere composed of densely packed filamentous cortical cells surrounding a tan core of parenchymal cells, where phenovariant B grew as a totally unorganized callus composed of parenchyma cells devoid of vascular elements or well-defined meristematic centers, shoots or leaves. Neither variant synthesized chlorophyll when grown under conditions of continuous lighting and variant A grew more slowly while variant B grew slightly faster than the parent organized tissue.

Glutamine-induced variation resulted in a phenotype indistinguishable from the snowy phenovariant with an occasional reversal to the parent organized phenotype depending on time between transfers and number of transfers on glutamine-containing medium. Malic acid, α -ketoglutaric acid, and ammonium ion promoted organized development while glutamine, glutamic acid, proline, γ -aminobutyric acid, aspartic acid and asparagine induced persistent changes to the snowy phenotype. These findings suggest that the reversible reaction of α -ketoglutaric acid and ammonium ion to form glutamic acid is a key site in regulating phenotypic expression in tobacco teratoma tissues.

- 1695 SPONTANEOUS CHOLANGIOMAS IN STRAIN C3H-A^{VY}AVYFB MICE AND IN THEIR HYBRIDS. (E.) Vlahakis, G. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.) and W. E. Heston. *J Nat Cancer Inst* 46(3):677-638, 1971.

Cholangiomas associated with bile ducts were seen in the livers of strain C3H-A^{VY}FB mice and in (C3H-A^{VY}FB X BALB/c) hybrids. The cholangiomas were seen only in animals which had also developed hepatomas. C3H-A^{VY}FB females produced 23 cholangioma-bearing mice out of 296 mice observed. Early cholangiomas often involved the epithelia of bile ducts in the liver; in one case, the cholangioma was seen in a bile duct which was contained in a hepatoma. Other early lesions appeared as proliferation of the small bile ducts. Better differentiated cholangiomas appeared to form ducts or acini. One of the cholangiomas was found to be malignant; it metastasized to the lung, and successfully underwent isogenic transplantation in 3 mice. The viable yellow gene and the lethal yellow gene were thought to be associated with the development of cholangiomas in these mice; these genes may have increased the susceptibility to cholangioma development of the mice.

- 1696 CARCINOMA OF THE LARGE INTESTINE WITH SURVIVAL IN A CHILD OF NINE AND IN HIS FATHER: A STUDY OF CARCINOMA OF THE COLON WITH PARTICULAR REFERENCE TO CHILDREN. (E.) Pemberton, M. (Enfield Group Hosp., England). *Brit J Surg* 57(11):841-846, 1970.

A boy presented to the hospital with abdominal pain which was found to have been caused by a large adenocarcinoma of the colon infiltrating through the wall and involving the small bowel and the abdominal wall. The tumor was removed surgically, recurred about a year later, and was excised; the patient recovered satisfactorily. The patient's father, aged 43, also had a rectal carcinoma infiltrating the muscle coat; the tumor was removed, and the father recovered completely. In the case of the first patient, the colonic condition was originally misdiagnosed as apendicitis, and the frequency of mistaken diagnoses associated with colorectal carcinomas was thought to be high. Long-term survival in a child having colonic carcinoma was found to be rare in a review of the literature. It was thought that in cases of colorectal carcinoma in which the tumor infiltrates but does not metastasize, the prognosis may be favorable. Although there was no positive evidence for a genetic basis for

this father-son occurrence, cancer development in a young person suggests the possible involvement of hereditary factors.

- 1697 BURKITT'S LYMPHOMA WITH FEMALE KARYOTYPE IN AN AFRICAN MALE CHILD. (E.) Manolov, G. (Inst. Genet., U. Lund, Sweden), A. Levan, J. S. Nadkarni, J. Nadkarni and P. Clifford. *Hereditas* 66(1):79-100, 1970.

A Burkitt's lymphoma tumor with a female karyotype was observed in a male African child who died of a left maxillary tumor with kidney involvement at age 9. Six chromosome fixations prepared from biopsies of the tumor showed a female karyotype for the tumor cells. Chromosome numbers recorded in the fixations were usually 45 or 46, with some counts as low as 43 and some as high as 48. Of 90 karyotype analyses available, 88 belonged to the tumor; of these, 87 were diploid, and 1 was hypotetraploid. The remaining 2 karyotypes were of bone marrow cells, and showed normal male karyotype. The C group of chromosomes had 16 chromosomes and the G group had 4, with the Y chromosome missing. Autoradiography showed 1 late-replicating X chromosome in the tumor cells. The chromosome lacking in the G group was thought to be the Y; no typical Y chromosome was ever seen in the tumor cells. The possibility that the tumor cell cultures had been contaminated, resulting in a female karyotype, was eliminated by the presence in all fixations of a characteristic small marker G chromosome. Transmission of cells from mother to child might account for the female karyotype tumor found in a male patient in this case.

- 1698 REGIONAL BIOENERGETIC EVENTS IN THE EXPERIMENTAL GLIOBLASTOMA: A QUANTITATIVE HISTOCHEMICAL STUDY. (E.) Kirsch, W. M. (U. Colorado Med. Sch., Denver) and D. R. Schulz. *J Neurosurg* 34(3):448-451, 1971.

Biochemical events occurring in a chemically induced murine glioblastoma during anaerobiosis were observed. The tumor responded to deprivation of oxygen more sluggishly than normal mouse brain tissue. Throughout the area of the glioblastoma, the production of lactate far exceeded expected levels; despite prolonged ischemia, all zones of the tumor continued to generate lactate and to maintain low but significant levels of ATP, suggesting the mobilization by the tumor of an unsuspected reserve of energy. A decrease in pentose nucleic acids was observed during prolonged ischemia in all zones of the tumor, the decrease was more pronounced in the periphery of the tumor than in its center. This finding suggests that the source of the hypothetical reserve energy in the tumor may be the nucleic acids, perhaps tumor RNA. Since the glioblastoma was virtually without capillaries, it was thought that nutrition of the tumor occurred exclusively from its surface.

- 1699 A CASE OF BURKITT'S TUMOR IN ITALY. (E.) Grampa, G. (U. Milan Med. Sch., Italy), M. Bestetti-Bosisio, F. Bergamini and P. Arlotta. *Path Europ* 5(4):470-484, 1970.

An 11-yr-old Italian boy presented to the hospital with large tumors of the oral cavity and a slight protrusion of the right eye. Biopsy of the tumor material confirmed the diagnosis of stem cell Burkitt's lymphoma, which was thought to be the first such diagnosis in Italy. Enlargement of the left testis due to tumor tissue, and a nodule at the root of the nose were additional features of the case which proved fatal 5 months after onset of symptoms. Tumor tissue was found to have invaded the brain on autopsy. Cytogenetic analysis of tumor cells showed a chromosome number ranging from 42-49, and the presence of an extra long acrocentric chromosome replacing one D-chromosome, and an extra C-chromosome with the characteristics of a number 10 chromosome. Inoculation of tumor cells in PPLO media produced a mycoplasma strain, later identified as *Mycoplasma orale*.

- 1700 ACHALASIA AND CARCINOMA OF THE ESOPHAGUS. (E.) Wychulis, A. R. (Mayo Grad. Sch. Med., Rochester, Minn.), G. L. Woolam, H. A. Andersen and F. H. Ellis, Jr. *JAMA* 215(10):1638-1641, 1971.

The development of carcinoma confirmed by esophageal roentgenograms and histologic analysis in patients treated for achalasia (1,318) from January, 1935 to January 1967 has been evaluated. Twelve men and one woman, ranging in age from 36 to 81 yr, developed esophageal carcinoma; they had been treated initially by simple dilatation with metal sounds from 1 to 12 times while 6 had also undergone hydrostatic dilatation 1-9 times; 3 had been treated surgically. In 10 of 12 patients with dysphagia an increase in intensity of symptoms was noted with concomitant hematemesis or melena or both. Malignant tumors arose at all levels of the esophagus and were diagnosed as 8 grade 3 (Broders') squamous cell carcinomas, 2 grade 1 verrucous squamous cell carcinomas and 1 grade 4 adenocarcinoma involving the cardia of the stomach. Duration of achalasia prior to diagnosis of carcinoma averages 28 yr. The incidence of carcinoma in this series of patients with achalasia is much lower than that reported by others, but is higher than the incidence of esophageal carcinoma in the general population, ranging from 16-84/100,000/yr as compared to 6/100,000/yr for the general population. Prognosis of esophageal carcinoma which arises from achalasia is poor because the extent and spread of the growth usually preclude the possibility of a curative surgical procedure.

- 1701 THE TRANSMISSION OF TUMORS INDUCED IN COCKROACHES BY NERVE SEVERANCE. (E.) Nayar, K. K. (Dept. Zool., Kerala U., Trivandrum, India), E. Arthur and M. Balls. *Experientia* 27(2):183-184, 1971.

Cell-free extracts from tumor tissue produced in the salivary glands, gastric ceca and receptacles of cockroaches by transection of the recurrent nerve

were injected into the hemocoel of normal cockroaches via the prothorax or abdominal tergite; cockroach nymphs in the final instar also received injections. Pronounced hemocyte invasion was observed in the salivary glands of most insects given injections of cell-free extract; hemocyte accumulation in the salivary glands was most pronounced in nymphs and in adults given tumor filtrate (450 nm filter); in general, nymphs developed more pronounced hemocyte accumulations than adults. Normal tissue extract produced no hemocyte invasion. Cytoplasmic granules which may have been hemocyte remnants were seen in the hemocytes accumulated in the glands.

- 1702 STUDIES OF THE AFFINITY OF NUCLEAR MATERIAL FOR UROPORPHYRIN: I. THE NUCLEI AND CHROMOSOMES OF EHRICH ASCITES TUMOR CELLS. (E.) Miya, K. (Dept. Med., U. Minnesota, Minneapolis), G. R. Hartmann, W. Runge and C. J. Watson. *Biochem Med* 4(5-6):391-402, 1970.

The uptake of uroporphyrin I *in vivo* and *in vitro* the nuclei and chromosomes of Ehrlich ascites tumor cells was studied in female mice of the Heston strain utilizing fluorescence microscopy with dark-field illumination or phase-contrast microscopy. The majority of the cells and particularly the nuclei exhibited fluorescence following i.p. injection of uroporphyrin I, with strong fluorescence exhibited in the ascitic fluid during the first 12 hr. In colchicine-treated animals, striking red fluorescence of metaphase chromosomes was most easily seen. The uroporphyrin was excreted completely from the ascitic fluid 20-24 hr after injection; however, most nuclei continued to fluoresce quite strongly up to 48 hr. When the agent was complexed with zinc, the results were similar to those of the free chemical. The nuclei of some cells from mice receiving uroporphyrin *in vivo* fluoresced more strongly than did the nuclei themselves.

- 1703 PARTITION OF ENERGY EXPENDITURE BETWEEN HOST AND TUMOR. (E.) Morrison, S. D. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.). *Cancer Res* 31(2):98-107, 1971.

Partition of energy metabolism between host and Walker tumor have been analyzed in adult male Sprague-Dawley rats utilizing oxygen consumption-carbon dioxide production monitoring. Total 24-hr energy expenditure per rat increased with increase in wt of the total organism with a precipitous decline in total energy expenditure in the terminal stage of tumor growth. The average total 24-hr energy expenditure before transplant in 12 animals ranged from 39.8-50.5 Kcal with the mean activity compartment ranging from 21.2%-28.2% compared to a range of 23.6-60.4 Kcal and a mean activity compartment of 11.9%-25.6% at the end of the tumor growth period. A linear relationship existed between tumor energy cost estimated from the constant activity of the host and the estimate of metabolizing tumor size. This study showed no evidence of a consistent rise in resting metabolism during tumor growth.

- 704 ON THE ORIGIN OF EWING'S TUMOR. (E.) Kadin, M. E. (Stanford U. Sch. Med., Calif.) and K. G. Bensch. *Cancer* 27(2):257-273, 1971.

A specimen of Ewing's tumor, resected from the leg of a 10-yr-old boy, was examined electron microscopically and maintained in tissue culture. The tumor had infiltrating margins, and neoplastic cells could be found beneath and within the vascular endothelium. Under electron microscopy, a striking feature of the tumor was the presence of large amounts of glycogen in the tumor cells, together with scarcity of other cytoplasmic organelles. Cell membranes were partially or altogether absent near zones of necrosis. In culture, the tumor tissue showed the growth pattern of a malignant mesenchymal tumor; there was a gradation in cell shape from round to narrow and spindle-shaped. Elongate cells contained relatively little cytoplasmic glycogen compared to the more rounded cells. In some clones of cells growing for more than 3 wk, multiple prominent Golgi zones were found which were characteristic of developing myelocytes. Alkaline phosphatase activity was minimal in elongate cells and notable in rounded cells; acid phosphatase was demonstrable only in cells which had been in tissue culture for long periods. Tumor cells showed no esterase activity. The findings appear to suggest that Ewing's tumor is a neoplasm of myelogenous origin with a growth and proliferation pattern similar to plasma cell myeloma.

- 705 FIBROADENOMAS IN THE BREAST OF JUVENILES. (E.) Ashikari, R. (Mem. Hosp. Cancer Allied Dis., New York, N. Y.), J. H. Farrow and S. O'Hara. *Surg Gynec Obstet* 132(2):259-262, 1971.

The pathology of mammary fibroadenomas developing in adolescent girls was examined in 181 hospital cases. Of these tumors, 169 were classified as the adult type, and 12 as the juvenile type lesion. The patients ranged in age from 10-20 yr. Fibroadenomas in juveniles were usually solitary and larger than fibroadenomas of the adult type; the largest tumor observed measured 19 cm. Microscopically, numerous irregularly proliferating duct-like and tubular structures were seen in the tumors; the stroma were dense, and more cellular than in adult type fibroadenomas. Mucinous degeneration and osseous metaplasia were also uncommon. Juvenile type fibroadenomas were always benign.

- 706 A STUDY OF THE ENDOMETRIUM IN INTRAUTERINE CONTRACEPTIVE DEVICE USERS. (E.) Rimdusit, S. (Siriraj Hosp., Bangkok, Thailand), A. Koetsawang, S. Tanapongpipatana and D. Rajawat. *Med Ass Thailand* 53(12):843-847, 1970.

The endometria of 210 users of intrauterine contraceptive devices (IUD) were examined by biopsy to determine the prevalence of malignant or premalignant changes in the endometrial tissue of IUD users. The study population ranged in age from 17-46; their parity ranged from 1-9. Of the 210 women, 112 were symptom-

free and 98 were symptomatic; no malignancy was found. There were 9 cases of endometrial hyperplasia and 27 cases in which the endometrial pattern involved a proliferative or secretory condition with lymphocyte or polymorphonuclear leucocyte infiltration. Most of the patients with endometrial hyperplasia were under 30-yr-old.

- 1707 OSTEOSARCOMA DEVELOPING IN SOLITARY ENCHONDROMA OF THE TIBIA. (E.) Rockwell, M. A. (Coll. Med., U. Florida, Gainesville) and W. F. Enneking. *J Bone Joint Surg* 53(2):341-344, 1971.

- 1708 CARCINOMA OF THE BILIARY TRACT COMPLICATING CHRONIC ULCERATIVE COLITIS. (E.) Morowitz, D. A. (Washington Hosp. Ctr., D. C.), S. Glagov, E. Dordal and J. B. Kirsner. *Cancer* 27(2):356-361, 1971.

- 1709 SIMULTANEOUS OCCURRENCE OF CONGENITAL ANIRIDIA, HAMARTOMA, AND WILMS' TUMOR. (E.) Haicken, B. N. (U. Rochester Sch. Med. Dent., N. Y.) and D. R. Miller. *J Pediatr* 78(3):497-502, 1971.

- 1710 NORMAL CHROMOSOMES IN MUCOSAL NEUROMA VARIANT OF MEDULLARY THYROID CARCINOMA SYNDROME. (E.) Nankin, H. (Montefiore Hosp., Pittsburgh, Pa.), J. Hydovitz and J. Sapira. *J Med Genet* 7(4):374-378, 1970.

- 1711 GASTRIC CARCINOMA DEVELOPING AFTER SURGERY FOR PEPTIC ULCER. (E.) Graves, H. A., Jr. (Vanderbilt U. Sch. Med., Nashville, Tenn.) and J. L. Herrington, Jr. *Amer Surg* 37(2):73-76, 1971.

- 1712 FAMILIAL HEPATOMA WITH HEPATITIS-ASSOCIATED ANTIGEN. (E.) Denison, E. K. (John Wesley County Hosp., Los Angeles, Calif.), R. L. Peters and T. B. Reynolds. *Ann Intern Med* 74(3):391-394, 1971.

- 1713 CHROMOSOMAL ANOMALIES IN A CASE OF PLASMOCYTIC LEUKEMIA. (Fr.) Cardini, G. (Reunis Hosp. Verbania, France), M. Bersi and C. Gasparini. *Nouv Rev Franc Hemat* 10(6):787-792, 1970.

- 1714 ULTRASTRUCTURAL FEATURES OF FOLLICULAR AND PAPILLARY CARCINOMAS OF THE THYROID. (Sp.) Gonzalez-Licea, A. (Nat'l. Med. Ctr., I.M.S.S., Mexico City, Mexico) and J. H. Yardley. *Arch Invest Med* 1(3):231-242, 1970.

1715 HYBRIDIZATION OF TWO CHINESE HAMSTER CELL LINES OF DIFFERENT CARCINOGENIC POTENCY. (Fr.) Berebbi, M. (Natl. Ctr. Sci. Res., Marseilles, France) and G. Barski. *C R Acad Sci* 272(2):351-354, 1971.

1716 THE ASSOCIATION OF OBESITY, HYPERTENSION, DIABETES MELLITUS AND CARCINOMA OF THE CORPUS UTERI. (Ger.) Haldemann, R. (U. Women's Clin. Berne, Switzerland). *Z Geburtshilfe Gynaek* 173(3):323-330, 1970.

1717 COMPARATIVE CHARACTERISTICS OF PHYSICO-CHEMICAL PROPERTIES OF DNA OF NORMAL AND MALIGNANT MOUSE FIBROBLASTS IN TISSUE CULTURE. (Rus.) Kuzmina, S. V. (Inst. Biol. Phys., Pushchino, Moscow Reg., U.S.S.R.) *Biofizika* 15(6):1133-1136, 1970.

1718 HODGKIN'S DISEASE AND HEPATOMA. (E.) Sahebji, H. (Washington Hosp. Ctr., D. C.). *South Med J* 64(1):117-118, 1971.

1719 FAMILIAL TRANSMISSION OF A Gq- Ph¹-LIKE) CHROMOSOME. (E.) Ricci, N. (Med. Clin. U. Ferrara, Italy), B. Dallapiccola and G. Preto. *Ann Genet* 13(4):263-264, 1970.

1720 PROLIFERATION KINETICS OF PHYTOHEMAGGLUTININ STIMULATED LYMPHOCYTES FROM PATIENTS WITH CHRONIC LYMPHADENOSIS AND LYMPHOGRANULOMATOSIS. (G) Pappas, A. (Med. Clin. U. Cologne, Germany), K. J. Lennartz, P. G. Scheurlen and H. Freyberger. *Med Welt* 22(4):123-127, 1971.

1721 AN UNUSUAL FORM OF MYELOID LEUKEMIA IN MAN: CHRONIC DEVELOPMENT, THE PRESENCE OF THE PHILADELPHIA CHROMOSOME AND LOSS OF THE Y CHROMOSOME IN THE MYELOID CELLS. (Fr.) Bauters, F. (Calmette Hosp., Lille, France), M. F. Croquette, Y. Delmas-Marsalet, M. Deminatti and M. Goudemand. *Nouv Rev Franc Hemat* 10(6):697-708, 1970.

1722 PULSE CYTOPHOTOMETRY OF DNA IN SKIN TUMORS. (Ger.) Schumann, J. (Westfälische Wilhelms-Universität, Münster, Germany), F. Ehring, W. Göhde and W. Dittrich. *Arch Klin Exp Derm* 239(4):377-389, 1971.

AUTHOR INDEX

AARONSON, S.A.
1528
ABDALLA, A.M.
1505, 1508
ABELSON, H.T.
1443
ABERNATHY, C.
1647
ABLASHI, D.V.
1434
ACHONG, B.G.
1423
ACKERMANN, W.W.
1431
ADAMCOVA, B.
1488
ADAMS, M.L.
1644
AGEYEV, A.K.
1271
AGRANAT, V.Z.
1634*
ALBOT, G.
1592, 1599*
ALEKSANDROWICZ, J.
1276
ALEKSEEV, I.V.
1290
ALEXANIAN, R.
1576
ALFORD, C.A., JR.
1460
ALONSO, A.
1372*
ALTHOFF, J.
1351
ALTWEIN, J.
1613
ALVAREZ, Y.
1501
AMATRUDA, J.
1653
AMOS, D.B.
1542
ANDERER, F.A.
1497
ANDERSEN, H.A.
1700
ANDERSON, C.K.
1579
ANDERSON, J.
1417
ANDERSSON, B.
1544
ANDRIANOVA, M.M.
1272, 1290
OKI, T.
1427
RAKI, M.
1357, 1358
RCHAMBEAU, J.O.
1384, 1385
RCHAMPONG, E.Q.
1416
RLOTTA, P.
1699

ARMSTRONG, J.A.
1428
ARORA, G.D.
1624
ARQUETE, J.
1516*
ARTHUR, E.
1701
ASHIKARI, R.
1705
AUBERT, C.
1328
AUGER, C.
1631*
AWANO, I.
1414
AYRES, J.L.
1308
AZERAD, E.
1279
BAARS, A.
1366
BACKMANN, B.
1307
BAILEY, J.M.
1655
BALDWIN, R.W.
1550
BALFOUR, H.H., JR.
1518*
BALLS, M.
1701
BALTIMORE, D.
1446
BANFIELD, W.G.
1635
BANNASCH, P.
1352
BARBER, R.
1605
BARINSKIY, I.F.
1418
BARKER, S.T.
1431
BARNES, D.W.H.
1381
BARSKI, G.
1715*
BARSTOW, M.C.
1474
BASILICO, C.
1513
BASSIR, O.
1309
BAUTERS, F.
1721*
BECHT, H.
1497
BECKER, F.F.
1299, 1303
BELICZA, M.
1671
BELL, J.A.
1673
BENJAMIN, S.A.
1522

BENSCH, K.G.
1704
BENYESH-MELNICK, M.
1532, 1693
BERARD, C.W.
1434, 1539
BEREBBI, M.
1715*
BERG, J.
1621
BERGAMINI, F.
1699
BERGER, R.
1280
BERGOLZ, V.M.
1448, 1477
BERNSTEIN, I.D.
1555
BERRY, G.
1610
BERSI, M.
1713*
BERTHOLON, J.
1374*
BERTINO, J.
1653
BERTRAND, J.
1642
BESKID, M.
1654
BESTETTI-BOSISIO, M.
1699
BETH, E.
1427
BETTINGER, H.F.
1282
BHATT, P.N.
1461
BIANO, G.
1548
BIERWOLF, D.
1426
BIRBECK, M.S.C.
1680
BISHOP, J.M.
1487
BISHUN, N.P.
1364
BLAIR, P.B.
1530
BLAIR, R.
1291
BLAKE, B.J.
1464
BLASCHECK, J.A.
1319
BLOMGREN, H.
1544, 1573
BLUNCK, J.M.
1316
BOCHAROV, A.F.
1418
BOEHM, N.
1640
BOGAKT, B.
1321

BOHUON, C.
 1328
 BOIRON, M.
 1476
 BOLOGNESI, D.P.
 1485
 BONHAG, R.S.
 1530
 BOONE, C.W.
 1500
 BORSOS, T.
 1555
 BOSMANN, H.B.
 1641
 BOTTGER, M.
 1426
 BOTTIGER, M.
 1495
 BOURRET, J.
 1370
 BOURSE, R.
 1375*
 BOYSE, E.A.
 1427
 BRAYLAN, R.C.
 1442

 BRENNAN, M.J.
 1419
 BRENNEIS, H.J.
 1385
 BRESNICK, E.
 1337, 1341
 BROCKMAN, W.W.
 1444
 BROMFELD, E.
 1446
 BROOKS, A.L.
 1394
 BROSS, I.O.J.
 1604
 BROWN, B.L.
 1548
 BRUGERE, J.
 1628*
 BUELL, D.N.
 1435
 BUESCHER, H.
 1692
 BUFTE, D.
 1577
 BUJADOUX, M.
 1547
 BULAY, O.M.
 1332
 BURG, C.
 1547
 BURGER, C.L.
 1474
 BURGER, D.R.
 1324
 BURGER, M.
 1657
 BURKITT, D.P.
 1608
 BURMESTER, B.R.
 1465, 1467

BURN, C.
 1607
 BURNS, E.R.
 1663
 BURROWS, J.H.
 1419
 BURTIN, P.
 1577
 BUSCHER, T.J.
 1454
 BUSTAD, L.K.
 1274
 BUTEL, J.S.
 1455, 1525
 BUXTON, D.F.
 1663

 CAEN, J.
 1643
 CAJAL, N.
 1490, 1498
 CANTY, T.G.
 1531, 1559
 CARBONE, G.
 1584
 CARBONE, P.P.
 1434
 CARDINI, G.
 1713*
 CARLSSON, C.A.
 1567
 CAROLI, J.
 1598*
 CARR, T.E.F.
 1381
 CARTER, A.P.
 1632*
 CARTER, R.L.
 1680
 CARTER, W.A.
 1444
 CATOVSKY, D.
 1365
 CEGLOWSKI, W.S.
 1529, 1534, 1535
 CENTENO, J.V.
 1689
 CESARINI, J.P.
 1421
 CHAMBERLAIN, C.C.
 1474
 CHANDRA, P.
 1551
 CHANDRASEKHARA, N.
 1305
 CHANG, L.O.
 1652
 CHANG, S.S.
 1543
 CHARNEY, J.
 1419
 CHAWDRY, I.
 1338
 CHEN, K.K.
 1293

 CHERKASSKIY, L.A.
 1586

CHEVREL, B.
 1598*
 CHEW, E.C.
 1665
 CHIHARA, G.
 1583*

 CHIVOT, J.J.
 1643
 CHO, H.Y.
 1326
 CHOI, Y.S.
 1667
 CHOPRA, H.C.
 1420, 1427, 1428
 CHRISTINE, B.W.
 1611
 CHU, E.H.Y.
 1393
 CHUAT, J.C.
 1476
 CIKES, M.
 1445
 CIOVIRNACHE, M.
 1297
 CLAPP, N.K.
 1348
 CLARK, C.G.
 1416
 CLARK, H.F.
 1425
 CLASON, A.E.
 1440
 CLEAVER, J.E.
 1388
 CLEMMESSEN, J.
 1267
 CLIFFORD, P.
 1423, 1697
 COFFEY, C.B.
 1317
 COHEN, J.J.
 1616
 COHN, M.
 1568
 COLE, P.
 1618
 COLMERAUER, M.E.M.
 1442, 1557
 CONE, C.D., JR.
 1269
 CONE, C.E., JR.
 1677
 CONNELL, D.I.
 1322
 CONNELLY, R.R.
 1612
 CONNEY, A.H.
 1334, 1335
 CONSIGLI, R.A.
 1511
 CONVENTI, L.
 1517*

 COOK, P.J.
 1608
 COOPER, E.H.
 1300, 1579

* indicates a plain citation without accompanying abstract

COOPERBAND, S.R.
1574
COUER, P.
1374*
COWAN, L.B.
1614
COWEN, D.M.
1300
CRAFT, J.L.
1461
CRAIG, N.C.
1659
CREECH, C.
1435
CREMER, N.E.
1447
CROISIER, J.C.
1279
CROQUETTE, M.F.
1721*
CUNNINGHAM, C.H.
1467
CZACHOR, M.
1276
CZAPIK, J.
1600*
DALEZIOS, J.
1310
DALLAPICCOLA, B.
1719*
DAMJANOV, I.
1671
DANIEL, M.D.
1464
DARJALOVA, S.L.
1634*
DAVIDSON, H.
1315
DAVIES, J.N.P.
1607
DAWE, C.J.
1273, 1512
DAYTON, S.
1363
DE BARBIERI, A.
1506
DE FLORIO, B.
1635
DEGTYARENKO, V.I.
1526
DEKNUDT, G.
1392
DELAIN, E.
1436
DELESCLUSE, C.
1516*
DELFS, E.
1653
DELLA ROSA, R.J.
1274
DELMAS-MARSALET, Y.
1721*
DE MADRID, A.T.
1428
DEMENT'YEV, I.V.
1418

DEMINATTI, M.
1721*
DENEKAMP, J.
1409*
DENISON, E.K.
1712*
DE-THE, G.
1481
DE TKACZEWSKI, L.Z.
1442
DEUTSCHER, S.
1625
DEY, A.K.
1292
DI PAOLO, J.A.
1322, 1331
DILLARD, R.D.
1287
DILLEY, W.G.
1676
DITTRICH, W.
1722*
DOBROTA, M.
1636
DOCHERTY, J.J.
1463
DODGE, O.G.
1607
DONATI, E.
1401*
DONOVAN, P.J.
1331
DONTENWILL, W.
1366
DORDAL, E.
1708*
DOSNE PASQUALINI, C.
1442, 1557
DOUGLAS, J.R.S.
1681
DUNBAR, L.M.
1655
DZHIOEV, F.K.
1320
EASON, R.
1492, 1494
EHRING, F.
1722*
EISENBERG, H.
1612
EL-FIKY, S.M.
1469, 1470
ELLIOTT, S.C.
1451
ELLIS, F.H., JR.
1700
ELSASSER, P.
1570
ELWOOD, J.C.
1651
EMAFO, P.O.
1309
EMARA, A.M.
1277
EMBLETON, M.J.
1550

EMERY, E.W.
1409*
ENNEKING, W.F.
1707*
ENOMOTO, M.
1359
EPSTEIN, M.A.
1423
EPSTEIN, S.M.
1296
ESCOURROLLE, R.
1402*
ESHBACH, T.B.
1504
ESTES, M.K.
1502
EVANS, E.P.
1381
FAIRCHILD, R.G.
1385
FALZI, G.
1404*
FANSHIER, L.
1487
FARBER, E.
1296
FARROW, J.H.
1705
FAYS, J.
1601*
FELDMAN, R.
1330
FELMEISTER, A.
1338
FENYO, E.M.
1445
FERRARA, A.
1690
FERRIERE, G.
1402*
FIALKOW, P.J.
1687
FIEL, R.J.
1430
FIELD, S.B.
1409*
FILATOV, F.P.
1418
FLOYD, R.
1532
FLOYD, W.S.
1619
FOLKMAN, J.
1647
FRANTSI, C.
1454
FRASER, E.E.
1683
FRAUMENI, J.F.
1603
FREYBERGER, H.
1720*
FREZOULS, G.
1438
FRIBERG, S.
1445

FRIEDMAN, E.W.
 1408*
 FRIEDMAN, H.
 1529, 1534, 1535
 FRIEDMAN, L.
 1275
 FRIESEN, H.G.
 1653
 FRIIS, R.R.
 1439, 1478, 1479
 FRITSCH, P.
 1368
 FROMBERG, D.
 1636
 FUJIWARA, K.
 1383
 FUKUOKA, F.
 1357
 GADOMSKA, H.
 1629*
 GADRAT, J.
 1375*
 GAIL, M.H.
 1500
 GALTON, D.A.G.
 1365
 GARANCIS, J.
 1653
 GARAPIN, A.C.
 1487
 GARCIA, F.G.
 1464
 GARCIA, H.
 1330
 GARDNER, M.B.
 1441
 GARTLER, S.M.
 1687
 GASCOIGNE, R.H.
 1616
 GASPARINI, C.
 1713*
 GAULDEN, M.E.
 1391
 GAUTIERI, R.F.
 1339
 GAVOSTO, F.
 1281
 GAZDAR, A.F.
 1443
 GAZZOLO, L.
 1481
 GEBHART, E.
 1360
 GEDER, L.
 1493
 GERARD-MARCHANT, R.
 1371, 1436
 GERGELY, L.
 1445
 GERICKE, D.
 1286, 1551
 GEY, G.O.
 1653
 GIACOMETTI, G.
 1506

GIBEL, W.
 1285
 GIBSON, R.
 1604
 GIBSON, W.R.
 1287
 GILSON, J.C.
 1610
 GIRALDO, G.
 1427
 GIRARD, R.
 1370, 1374*
 GIUNTA, J.L.
 1541
 GLAGOV, S.
 1708*
 GOEHDE, W.
 1722*
 GOELZER, M.L.
 1545
 GOERTTLER, K.
 1349
 GOERTZ, E.
 1366
 GOH, K.O.
 1688
 GOLDBERG, R.J.
 1463
 GOLDENBERG, H.
 1327
 GOLDSCHMIDT, B.M.
 1291
 GOLDSTEIN, M.N.
 1684
 GONZALEZ-LICEA, A.
 1714*
 GORDON, H.L.
 1429, 1430
 GOSSEREZ, M.
 1601*
 GOTLIEB-STEMATSKY, T.
 1519
 GOUEMAND, M.
 1721*
 GOULD, V.E.
 1378*
 GRAF, B.
 1410*
 GRAF, T.
 1485
 GRAF, W.
 1333
 GRAFFE, L.H.
 1490, 1498
 GRAFFI, A.
 1426
 GRAHAM, C.E.
 1294
 GRAHL-NIELSEN, G.
 1673
 GRAMPA, G.
 1699
 GRANDE, P.
 1630*
 GRAVES, H.A., JR.
 1711*

GREEN, H.
 1507
 GREGORY, K.F.
 1454
 GREY, H.M.
 1568
 GRILLI, S.
 1362
 GRIMLEY, P.M.
 1635
 GROUPE, V.
 1472
 GRUENSTEIN, M.
 1327
 GRUPPER, C.
 1516*
 GRYNBLAT, A.
 1598*
 GUALANDRI, V.
 1284*
 HAAG, D.
 1349
 HABER, S.
 1335
 HAGLID, K.G.
 1567
 HAGUENAU, F.
 1484
 HAHN, E.E.A.
 1524
 HAICKEN, B.N.
 1709*
 HALDEMANN, R.
 1716*
 HALLIDAY, W.J.
 1554
 HAMMOND, W.G.
 1635
 HAMPAR, B.
 1521
 HANNA, C.
 1663
 HARAN-GHERA, N.
 1325
 HAREL, J.
 1438
 HAREL, L.
 1438
 HARKE, H.P.
 1366
 HARRIS, J.
 1576
 HARRIS, P.N.
 1287, 1293
 HARTENSTEIN, R.
 1350
 HARTMANN, G.R.
 1572, 1702
 HASEGAWA, K.
 1515
 HATAKEYAMA, S.
 1319
 HATANO, T.
 1590
 HAUGHTON, G.
 1540

* indicates a plain citation without accompanying abstract

HAUNG, A.T. 1542	HOROSZEWICZ, S.J. 1433	JANZEN, H.W. 1661
HAUSE, L. 1653	HOSHINO, K. 1665	JAPRETT, O. 1440
HAWTHORNE, C. 1563	HOSHINO, T. 1398, 1399	JASTY, V. 1459
HAY, J. 1440	HOSOKAWA, M. 1533	JAYLE, M.F. 1313
HAYASHI, H. 1682	HOWARD, A. 1380	JENEY, E. 1493
HEARON, E.C. 1512	HOWARD, B.V. 1502	JENSEN, E.M. 1420
HECHT, F. 1570	HRABOWSKA, M. 1664	JILDEROS, B. 1645
HEILBRON, D. 1483	HSU, C.C.S. 1574	JONAS, A.M. 1461
HEINE, U. 1413	HSU, K.C. 1521	JONDORF, W.R. 1346
HENDRY, J.H. 1380	HUANG, W.Y. 1653	JONES, D.S. 1683
HERBERMAN, R.D. 1520, 1531	HUEBNER, R.J. 1326	JONES, E.E. 1548
HERRINGTON, J.L., JR. 1711*	HUGHES, N.R. 1569	JONES, N.D. 1644
HERSH, E. 1576	HULKA, B.S. 1620	JOYET, G. 1400
HESTON, W.E. 1471, 1695	HUNG, P.P. 1482	KADIN, M.E. 1704
HEYDER, J. 1403*	HUNT, R.D. 1464	KAJI, H. 1533
HEY-FERGUSON, A. 1341	HURST, L. 1313	KAKIZAWA, H. 1560
HIASA, Y. 1312	HYDOVITZ, J. 1710*	KALLNER, H. 1615
HIGGINS, M. 1535	ICHIMARU, M. 1398, 1399	KANG, H.S. 1504
HILF, R. 1327	IMAMURA, T. 1432	KAPLAN, P.M. 1457
HILLCOAT, B.L. 1646	INCH, W.R. 1675	KAREWICZ, Z. 1629*
HILSCHMANN, N. 1581*	IOACHIM, H.L. 1449	KATCHLASKI, E. 1377*
HINDRINGER, B. 1382	IONESCU-HOMORICEANU, S. 1490, 1498	KATZ, C. 1291
HINRICHS, D.J. 1324	IRISH, L.E. 1324	KAUL, A. 1403*
HINTON, R.H. 1636	IRVING, C.C. 1298, 1301	KAWASHIMA, K. 1560, 1658
HIRANO, M. 1560	ISHIMARU, T. 1398, 1399	KAWAZOE, Y. 1356, 1358
HIRSHAUT, Y. 1427, 1435	ISUZAKI, R. 1437	KAZANOVA, L.I. 1596
HIRST, J.W. 1568	ITO, N. 1312	KEIDITSCH, E. 1649
HLOZANEK, I. 1486	IWATA, A. 1511	KENYON, A.J. 1644
HOD, I. 1411	IZAWA, M. 1658	KETTERER, B. 1315
HOEFFEL, J.C. 1601*	JACKSON, C.D. 1298	KILLMANN, S.A. 1686
HOLGERSEN, L.O. 1591	JACKSON, J. 1483	KIM, C.A.H. 1553
HOLLEB, A.I. 1602	JAHNES, W.G. 1480	KIM, S.N. 1644
HOLMES, E.C. 1536	JANOWER, M.L. 1396	KING, C.M. 1306

KIRSCH, W.M.
1698
KIRSNER, J.B.
1708*
KIT, S.
1503
KLEIN, E.
1445
KLEIN, K.M.
1303
KLIETMANN, W.
1537
KLUBES, P.
1346
KNOPF, P.M.
1667
KNOTH, M.
1653

KNOWLES, J.C.
1300
KNUTSEN, T.
1512
KNYSZYNSKI, A.
1657
KOBAYASHI, H.
1533
KOBAYASHI, J.
1389, 1390
KOCH, M.A.
1497
KOERBLER, J.
1633*
KOETHE, W.
1593
KOETSAWANG, A.
1706
KOETSAWANG, S.
1706
KOFER, W.
1692
KOHEN, M.
1577
KONRAD, K.
1368
KOO, G.C.
1529, 1535
KORNITSKY, M.A.
1329
KOSIOROWSKA, J.
1415
KOSS, L.G.
1302, 1304
KOTTARIDIS, S.D.
1466
KOVACS, K.
1319
KOWALEWSKI, K.
1347
KOZLOWSKI, H.
1664
KRAMARSKY, B.
1419
KREIDER, J.W.
1522
KREMER, W.B.
1542

KRIPKE, M.
1558
KRIPIKE, M.L.
1530
KROGH JENSEN, M.
1686
KROH, H.
1342
KRUEGER, F.W.
1351
KRUEGER, G.
1589
KRUEGER, G.R.F.
1539
KRUSH, A.J.
1278
KUEHNERT, M.
1662
KUKAYN, R.A.
1473
KUNTZMAN, R.
1334, 1335
KURBANOV, A.
1596
KURTZ, H.
1431
KUSANO, T.
1507
KUTINOVA, L.
1509
KUZMINA, S.V.
1717*
LACASSAGNE, A.
1313
LACOUR, F.
1436
LAFUMA, J.
1410*
LAGHI, V.
1690
LAGRUTTA, J.
1585
LAGUENS, R.P.
1585
LAHIRI, B.
1624
LAM, K.W.
1637
LANZOLA, E.
1622
LAPIS, K.
1670
LAPPE, M.A.
1530
LASFARGUES, E.Y.
1419
LASQUELLEC, F.
1476
LAU, M.
1343
LAURENT, M.
1685
LAVIN, P.
1302, 1304

LAW, L.W.
1543

LAWSON, T.A.
1320
LEE, D.J.
1308
LEE, J.A.H.
1632*
LEE, L.F.
1465
LEE, S.K.
1578
LEHMANN, H.E.
1580*
LEMERLE, J.
1371
LENNARTZ, K.J.
1720*
LENNETTE, E.H.
1447
LENNOX, E.S.
1667
LEONARD, A.
1392
LEONG, J.
1487
LEUCHTENBERGER, C.
1367
LEUCHTENBERGER, R.
1367
LEVAN, A.
1697
LEVI, P.E.
1300
LEVINE, A.J.
1504
LEVINE, P.H.
1434, 1578
LEVINSON, W.
1483
LEVINSON, W.E.
1487
LEVY, J.A.
1435
L'HIRONDEL, A.M.
1476
LI, C.P.
1480
LI, C.Y.
1637
LI, L.H.
1444
LIJINSKY, W.
1330
LLOMBART, A., JR.
1373*

LLOYD, J.W.
1369
LORAS, B.
1642
LORENC, R.
1654
LOUTIT, J.F.
1381
LUBETZKI, J.
1279
LUCIAK, M.
1600*

LUGINBUHL, R.E.
 1466
 LUM, G.S.
 1412, 1424
 LURIE, M.
 1325
 LUTHRA, U.K.
 1624
 LUZ, A.
 1382
 LYNCH, H.T.
 1278
 LYON, G.
 1484
 MACA, R.A.
 1413
 MACEK, M.
 1693
 MACKOVA, V.
 1693
 MAC MAHON, B.
 1618
 MAC MAHON, C.E.
 1395
 MAC PHERSON, I.
 1514
 MAEDA, Y.Y.
 1583*
 MAHER, B.C.
 1474
 MAHI, P.N.
 1624
 MAIROSE, U.B.
 1613
 MAJUMDAR, S.K.
 1340
 MALAMUD, D.
 1674
 MALAN, L.
 1434
 MALHOTRA, S.L.
 1597
 MALLEIN, M.L.
 1374*
 MALMGREN, R.A.
 1539
 MALT, R.A.
 1674
 MANAKER, B.A.
 1413
 MANCINI, L.O.
 1459
 MANGUM, J.H.
 1496
 MANLY, K.F.
 1446
 MANN, D.E., JR.
 1339
 MANNERING, G.J.
 1344
 MANNING, M.D.
 1603
 MANOCHA, S.L.
 1294
 MANOLOV, G.
 1697

MANSELL, P.W.A.
 1423
 MARCUS, N.
 1598*
 MARINONI, A.
 1622
 MASON, M.M.
 1420
 MATSUYAMA, M.
 1354
 MATTINGLY, R.F.
 1653
 MAURER, B.A.
 1432
 MAXFIELD, W.S.
 1295
 MAZUROWA, N.
 1415
 MC BRIDE, R.Z.
 1317
 MC COLLESTER, D.L.
 1549
 MC CORMICK, K.J.
 1417
 MC CREDIE, J.A.
 1675
 MC REYNOLDS, D.G.
 1518*
 MEINS, F., JR.
 1694
 MELCHERS, F.
 1565
 MELCHIONNE, S.
 1291
 MELENDEZ, L.V.
 1464
 MELNICK, J.L.
 1455, 1457
 MELONI, G.A.
 1517*
 MERANZE, D.R.
 1327
 MERKOW, L.P.
 1296
 MERLER, E.
 1647
 METZGAR, R.S.
 1542
 MICHEL, H.
 1643
 MICHEL, I.
 1327
 MIETTINEN, O.S.
 1396
 MIGLIORE, P.
 1576
 MILLER, B.A.
 1431
 MILLER, D.R.
 1709*
 MILLER, L.T.
 1459
 MILLER, R.E.
 1591
 MILLER, R.W.
 1606

MILLMAN, P.A.
 1661
 MIRONESCU, S.
 1297, 1491
 MIRRA, A.P.
 1618
 MITAL, V.P.
 1624
 MITUS, W.J.
 1603
 MIURA, M.
 1560
 MIYAGI, K.
 1702
 MIYAMOTO, K.
 1521
 MODAN, B.
 1615
 MOHR, U.
 1345, 1351
 MOLONEY, J.B.
 1472
 MONNIER, J.
 1375*
 MONTI-BRAGADIN, C.
 1517*
 MOORE, D.H.
 1419, 1469
 MORAILLON, A.
 1484
 MORERA, A.M.
 1642
 MORGAN, C.
 1521
 MORGAN, W.D.
 1512
 MORGENROTH, K., JR.
 1307
 MORITA, A.
 1560
 MOROWITZ, D.A.
 1708*
 MORRIS, H.P.
 1651, 1652
 MORRISON, S.D.
 1703
 MORTON, D.L.
 1536
 MOSKOVKINA, O.YA.
 1448, 1477
 MOSLANDER, V.
 1614
 MULLOCK, B.M.
 1636
 MURPHY, W.H.
 1431
 MUSHINSKI, J.F.
 1564
 NACHTIGAL, M.
 1490, 1491, 1498
 NADKARNI, J.
 1697
 NADKARNI, J.S.
 1697
 NAGAKI, D.
 1515

NAGAYEVA, L.I.
 1473
 NAJARIAN, J.S.
 1582*
 NAKAJIMA, K.
 1503
 NAKAMURA, T.
 1354
 NAKAZAWA, I.
 1639
 NANKIN, H.
 1710*
 NARAYAN, K.A.
 1305
 NAYAN, R.
 1292
 NAYAR, K.K.
 1701
 NAZERIAN, K.
 1465
 NELSON, N.S.
 1274
 NELSON, R.L.
 1331
 NESBIT, M.E.
 1518*
 NEUHAUS, O.W.
 1386
 NEWELL, G.R.
 1617
 NEZELOF, C.
 1685
 NIAS, B.C.
 1607
 NICHOL, F.R.
 1444
 NILSSON, A.
 1379
 NISHIOKA, B.
 1627
 NISHIWAKI, H.
 1560
 NITAVSKAYA, S.D.
 1473
 NOBEL, T.A.
 1411
 NORTH, J.A.
 1496
 NOVOGRODSKY, A.
 1377*
 OCKEN, P.R.
 1321
 ODASHIMA, S.
 1353
 OGATA, K.
 1575
 O'HARA, G.P.
 1339
 O'HARA, J.
 1705
 OHNO, R.
 1560
 OJALA, A.
 1595
 OKADA, H.
 1398, 1399

OKANO, T.
 1355
 OLD, L.J.
 1427
 OLIVER, J.A.
 1505, 1508
 O'NEILL, R.T.
 1566
 OREN, M.E.
 1520, 1531
 OSHIRO, L.S.
 1447
 OSTRETSOVA, I.B.
 1288
 OTH, D.
 1547
 OTSU, H.
 1336
 OTTEN, J.A.
 1348
 OZAKI, T.
 1682
 PAGANO, J.S.
 1502
 PAOLETTI, C.
 1270
 PAPPAS, A.
 1720*
 PARDO, M.
 1296
 PARMENTIER, C.
 1410*
 PARMENTIER, N.
 1410*
 PARMIANI, G.
 1584
 PARTURIER-ALBOT, M.
 1592, 1599*
 PASQUALINI, C.D.
 1523
 PATRONO, C.
 1690
 PATTILLO, R.A.
 1653
 PAULUZZI, S.
 1456
 PAYMASTER, J.C.
 1419
 PEARCE, M.L.
 1363
 PEKAREK, J.
 1538
 PEMBERTON, M.
 1696
 PERCY, D.H.
 1461
 PERIMAN, P.
 1546
 PERK, K.
 1411
 PERTAYA, A.V.
 1526
 PESKOVA, V.I.
 1596
 PETERS, R.F.
 1394

PETERS, R.L.
 1712*
 PETRUN, A.S.
 1318
 PEYDRO, A.
 1373*
 PHILLIPS, B.
 1306
 PIERCE, G.B.
 1588
 PILCH, D.J.F.
 1450
 PILCH, Y.H.
 1561
 PINKHAS, J.
 1643
 PIRAS, A.
 1456
 PITTS, J.D.
 1440
 PLAINFOSSE, B.
 1371
 PLANTEROSSE, D.N.
 1450
 PODZEY, L.K.
 1314
 POIRIER, J.
 1402*
 POLLACK, R.
 1507
 POLONSKI, R.
 1664
 POLYZONIS, M.B.
 1669
 POMPLUN, S.
 1406*
 PONSSTINGL, H.
 1581*
 PORTERFIELD, J.S.
 1426
 PORAIT-BOBR, Z.
 1510
 POTVIN, R.
 1631*
 PRADE, M.
 1328
 PREHN, R.T.
 1584
 PRETO, G.
 1719*
 PRIS, J.
 1375*
 PRODI, G.
 1362
 PRUCHNIC, W.F.
 1522
 PRUNIERAS, M.
 1516*
 PRUTKIN, L.
 1321
 PTAK, W.
 1510
 PURCHASE, H.G.
 1467
 QUIJANO, F.
 1585

RABASA, S.L.
1523, 1557
RABES, H.
1350
RABINOVIC, JE.A.
1634*
RABOTTI, G.F.
1484, 1527
RABSTEIN, L.S.
1443
RADNOT, M.
1670
RAJ, H.G.
1311
RAJAWAT, D.
1706
RAMMING, K.P.
1561
RAPP, F.
1463
RAPP, H.J.
1555
RAPP, W.
1580*
RATCLIFFE, N.A.
1668
REDMOND, C.K.
1620
REES, E.D.
1340
REESE, A.B.
1666
REGNIER, M.
1516*
REICHEL, W.
1581*
REID, E.
1636
REIF, A.E.
1553

REISS, J.
1376*
RENAWEK, K.
1342
REUSSER, F.
1444
REYNOLDS, T.B.
1712*
RHIM, J.S.
1326
RICCI, N.
1719*
RICHARDSON, L.S.
1525
RICKARD, V.D.
1623
RIECHERS, L.A.
1322
RIGAS, D.A.
1570
RIGBY, P.G.
1556
RIGGS, V.
1563
RIMDUSIT, S.
1706

RIMOIN, D.L.
1687
RIOU, G.
1270
RITUCCI, A.
1404*
ROBBINS, P.W.
1514
ROBINSON, D.J.
1462
ROBINSON, H.L.
1482
ROBINSON, W.S.
1482
ROCCHI, P.
1362
ROCKWELL, M.A.
1707*
ROHRBACH, R.
1343
ROLLAG, M.D.
1394
ROSEN, S.W.
1656
ROSENOER, V.M.
1548
ROSS-MANSELL, P.
1315
ROUNDS, D.E.
1562

ROUSSEAU, M.F.
1685
ROWE, J.M.
1395
ROZENBLATT, S.
1499
RUBENCHUK, B.L.
1318
RUDOLPH, R.
1616
RUHENSTROTH-BAUER, G.
1387
RUMPLER, B.
1343
RUNGE, W.
1702
RUSH, M.G.
1492
RUSSO, A.
1404*
SAAL, F.
1523
SAEZ, J.M.
1642
SAGEBIEL, R.W.
1687
SAHEBJAMI, H.
1718*
SAHNAZAROV, N.
1490, 1491, 1498
SAITO, H.
1533
SAITO, M.
1515
SAITO, T.
1359

SALAS, J.
1507
SALZANO, F.M.
1689
SAMPSON, C.C.
1623
SAN, R.H.C.
1356
SANBE, M.
1414
SANDRITTER, W.
1640
SANEYOSHI, M.
1357
SANFORD, B.H.
1552
SAPIRA, J.
1710*
SARGENTINI, S.
1690

SARKAR, N.H.
1419, 1469
SASAKI, M.
1691
SATO, K.
1359
SATO, S.
1658
SCEVOLA, M.E.
1506
SCHACHT, U.
1352
SCHELLANDER, F.
1368
SCHERSTEN, T.
1645
SCHEURLIN, P.G.
1720*
SCHIFFER, A.
1276
SCHLEDE, E.
1334, 1335
SCHLOM, J.
1472
SCHLOSS, G.T.
1451
SCHMAHL, D.
1351
SCHMIDT, N.F.
1644
SCHNAITMAN, C.A.
1652
SCHNEIDER, W.C.
1660
SCHOLZE, P.
1350
SCHOTTENFELD, D.
1621
SCHRAMM, T.
1285
SCHREMMER, C.N.
1672
SCHULZ, D.R.
1698
SCHUMANN, J.
1722*

SCHWARZ, J.
1581*
SCHWEBACH, G.
1496
SCHWEISGUTH, O.
1371
SEEMAYER, N.
1537
SEGALOFF, A.
1295

SEIDEL, E.H.
1693
SEIGLER, H.F.
1542
SELKIRK, J.K.
1651
SENDO, F.
1533
SERINGE, P.
1371
SERRA, A.
1690
SETH, R.K.
1624
SHANKARAN, R.
1311
SHEDD, D.P.
1612
SHEVELEV, B.I.
1448
SHEYKIN, P.I.
1594
SHIHABI, Z.
1386
SHIMIZU, T.
1437
SHIMKIN, M.B.
1327
SHIMOJO, H.
1458
SHIRAI, T.
1533
SHKLAR, G.
1541
SHUBIK, P.
1330
SHUBLADZE, A.K.
1418
SILVERBERG, E.
1602
SILVERBERG, H.
1435
SIMKOVIC, D.
1488
SIMMONS, R.L.
1582*
SINGER, H.
1692
SINNHUBER, R.O.
1308
SIRSAT, S.M.
1419
SKREB, N.
1671
SLIFKIN, M.
1296

SLOW, I.N.
1408*
SMART, C.R.
1614
SMITH, G.H.
1422
SMITH, H.
1668
SMITH, J.B.
1566
SMOLER, D.F.
1446
SMYK, B.
1276
SNIDER, M.E.
1460
SOGA, J.
1590
SOLOFF, B.L.
1663
SOLTER, D.
1671
SONLEY, M.J.
1578
SOO, S.F.
1552
SOROF, S.
1317
SPEICHER, C.E.
1518*
SPRENGER, E.
1640
STANFORD, G.B.
1666
STARA, J.
1274
STEINBACH, K.H.
1405*
STENBACK, F.
1323, 1595
STENBACK, W.A.
1417
STERN, D.
1408*
STEVENS, D.A.
1466, 1578
STEVENS, D.F.
1563
STEWART, A.
1605
STICH, H.F.
1356
STOCK, J.A.
1680
STOLZMANN, W.M.
1678

STRAUCH, L.
1649
STRICKER, M.
1601*
STRIMLAN, C.V.
1522
STUBBS, K.G.
1460
SULLIVAN, P.D.
1611

SUNE, M.V.
1689
SUSANNA, L.
1622
SUTHERLAND, R.M.
1675
SUZUKI, E.
1458
SUZUKI, H.
1354
SVEDMYR, E.
1573
SVEJCAR, J.
1538
SWISHER, S.N.
1688
TAGUCHI, F.
1515
TAKADATE, A.
1355
TAKEICHI, N.
1533
TAKIZAWA, K.
1453
TALLENT, M.B.
1582*
TAMURA, M.
1358
TANAKA, T.
1579
TANAPONGPIPATANA, S.
1706
TANK, R.
1378*
TARNVIK, A.
1571
TASCA, C.
1349
TASHJIAN, A.H., JR.
1638
TASSI, G.C.
1506
TAURASO, N.M.
1480
TAYLOR, C.M.
1635

TEEBOR, G.W.
1299
TEITZ, Y.
1447
TEMIN, H.M.
1268
TEMPLETON, A.C.
1609
TER-GRIGOROV, V.S.
1448, 1477
TEUTSCH, B.
1527
TEVETHIA, S.S.
1455, 1457
THOMAS, C.
1343
THORNTON, J.
1391
THURSTON, O.G.
1661

* indicates a plain citation without accompanying abstract

TIMBRELL, V.	VIEGAS, O.A.C.	WELLER, D.L.
1610	1609	1563
TODD, E.F.	VINOGRAD, J.	WEPSIC, H.T.
1347	1492, 1494	1555
TOKUZEN, R.	VLAHAKIS, G.	WESSEL, W.
1357	1471, 1695	1679
TOLOT, F.	VOELKEL, E.F.	WEXLER, M.R.
1370, 1374*	1638	1558
TOMIYASU, T.	VOGT, P.K.	WHALLEY, J.M.
1398, 1399	1439, 1478	1440
TOTH, B.	VON ESSEN, C.F.	WHANG PENG, J.
1361	1612	1512
TOUSIMIS, A.J.	VONKA, V.	WHITE, D.A.
1635	1509, 1532, 1538	1504
TOYOSHIMA, K.	WACKER, A.	WIEGENSTEIN, L.
1312, 1478	1551	1378*
TREHEUX, A.	WAGGONER, D.E.	
1601*	1434, 1578, 1617	WILBERT, S.M.
TRENTIN, J.J.	WAGNER, J.C.	1432
1417	1610	WILLIAMS, A.E.
TRITSCH, G.L.	WAGNER, J.L.	1668
1673	1540	WILLIAMS, G.
TSUBURA, Y.	WAHLQUIST, L.	1647
1312	1645	WINOCOUR, E.
TSUCHIMOCHI, T.	WALES, J.H.	1499
1650	1308	WITTER, R.L.
TSUCHIMOTO, T.		1465
1398, 1399	WALLACE, A.C.	WIVEL, N.A.
TYNDALL, R.L.	1683	1422
1348	WALLACE, C.	WLODARSKI, K.
UCHIYAMA, M.	1588	1415
1639	WALLCAVE, L.	WOGAN, G.N.
UEKAMA, K.	1330	1310
1355	WANG, F.C.	WOLBERG, W.H.
UETANI, T.	1353	1545
1560	WANG, R.	WOOD, M.
UNGER, E.	1507	1300
1407*	WARD, F.E.	WOODSIDE, N.J.
	1542	1420
USHIJIMA, K.	WATCHI, J.M.	WOOLAM, G.L.
1682	1371	1700
VACZI, L.	WATSON, C.J.	WORTHINGTON, M.
1493	1572, 1702	1528
VAIDYA, A.B.	WATSON, D.H.	WUNDERLICH, J.R.
1419	1462	1559
VALENTIN, F.	WATTENBERG, L.W.	WUNDERLICH, V.
1601*	1332	1426
VALET, G.	WEBER, E.	WYCHULIS, A.R.
1387	1405*	1700
VALLADARES, Y.	WEGENER, K.	YAKOVLEVA, L.S.
1501	1397	1475
VAN DUUREN, B.L.	WEGNER, K.W.	YAM, L.T.
1291	1613	1637
VANSOVER, A.	WEILER, O.	YAMADA, K.
1519	1436	1560
VASS, W.	WEINER, N.D.	YAMAGATA, S.
1326	1338	1639
VEAZEY, R.A.	WEINREB, S.M.	YAMAMOTO, H.
1301	1310	1489
VEHASKARI, A.	WEINTRAUB, B.D.	YAMAMOTO, T.
1595	1656	1398, 1453
VENKITASUBRAMANIAN, T.A.	WEISS, D.W.	YARBRO, J.W.
1311	1558	1648
VESCO, C.	WEISS, L.	YARDLEY, J.H.
1513	1433	1714*
VETTO, R.M.	WEISS, W.	YATES, V.J.
1324	1626	1459

YEE, M.
1337
YEGHIAYAN, E.
1319
YERMOLOVA, T.S.
1586

YOKOTA, Y.
1587
YORAN, C.
1615
YOSHIDA, H.
1414
YOSHIDA, K.
1682
YOSHIDA, Y.
1515
YOSHIKURA, H.
1452
YOUNG, E.M.
1317

YOUNG, L.
1530
ZABEZHINSKIY, M.A.
1289
ZACHARIA, T.P.
1468
ZAHNERT, R.
1397
ZANG, K.D.
1692
ZANKL, H.
1692
ZAUCHE, A.
1628*
ZATSEPIN, N.I.
1526
ZAVADOVA, H.
1509, 1538
ZBAR, B.
1555
ZBYTNIIEWSKI, Z.
1283*

ZEIGEL, R.F.
1425, 1430
ZELLJADT, I.
1420
ZEMBALA, M.
1510
ZEMER, D.
1615
ZEPPA, M.P.
1456
ZHILEVICH, A.V.
1473
ZIELINSKI, J.
1600*
ZIMMER, S.
1662
ZINTEL, H.A.
1591

SUBJECT INDEX

- 2-ACETYLAMINOFLUORENE
 - METABOLITE, BINDING, RAT LIVER, NUCLEIC ACIDS (1301)
 - MOUSE, BLADDER, EPITHELIUM (1300)
- ACHALASIA
 - CARCINOMA, ESOPHAGUS (1700)
- ACTINOMYCIN D
 - PUROMYCIN, LYMPHOCYTES, PHYTO-HEMAGGLUTININ (1678)
- ADENOCARCINOMA
 - IMMUNOSUPPRESSION, THYMECTOMY, RADIATION, MICE (1552)
- ADOLESCENCE
 - MAMMARY FIBROADENOMAS (1705)
- ADRENAL GLAND
 - ADRENOCORTICAL VIRILIZING CARCINOMA, STEROIDS (1642)
 - HISTOCHEMISTRY, WHOLE BODY IRRADIATION, RAT (1407)*
 - NEUROBLASTOMA, ANTIGENS, FETUS, (1577)
- AFLATOXIN
 - B1, CHICK LIVER, CARBOHYDRATE METABOLISM (1311)
 - B1, ENZYME HISTOCHEMISTRY, MUCOR HIEMALIS FUNGUS (1376)*
 - B1, LIVER MICROSOME, REPTILE, FOWL (1309)
 - B1, RAT LIVER, TRANSFORMATION, IN VITRO (1312)
 - B1, STRUCTURE-ACTIVITY RELATIONSHIP, TROUT (1308)
 - MYCOTOXINS, BLOOD MALIGNANCIES, LIVER CARCINOMA (1276)
 - P1, MONKEY, AFLATOXIN METABOLITE (1310)
- AGE
 - BENZO(A)PYRENE, ORGANOTROPY, HUMAN (1333)
 - FIRST PREGNANCY, MAMMARY CARCINOMA, WEIGHT (1618)
 - URETHAN, TUMOR INDUCTION, HAMSTERS 1361
- AMINO ACID
 - ALPHA-AMINOISOBUTYRIC ACID UPTAKE, IRRADIATED RAT LIVER (1386)
 - COMPOSITION, T-ANTIGEN, ADENOVIRUS TYPE 12, HAMSTER (1526)
- ANILINE
 - RAT CORPOREA LUTEA, STEROIDOGENESIS (1319)
- ANTIBODY
 - IMMUNOGLOBULIN PRODUCTION, MURINE PLASMACYTOMA (1546)
 - MONKEY KIDNEY, SV40, VIRUS REPLICATION (1495)
 - MULTIPLE MYELOMA, KEYHOLE LIMPET HEMOCYANIN (1576)
 - RESPONSE, GROSS LEUKEMIA VIRUS, LYMPHOMA (1520)
 - SV40, LABORATORY MONKEY HANDLERS (1524)
- ANTIGEN
 - CHICK-EMBRYO-LETHAL-ORPHAN VIRUS, CHICK KIDNEY CELLS (1417)
 - COMMON ANTIGENICITY, ANEMIA-INDUCING PLACENTAL SUBSTANCE, MUCOPROTEIN IN URINE OF CANCER PATIENTS (1575)
 - COMMON ANTIGENICITY, MAMMARY TUMOR VIRUS, MOUSE (1536)
 - COMPLEX, AVIARY SARCOMA, ROUS SARCOMA VIRUS (1527)
 - CROSS-REACTIVITY, MAREK'S DISEASE, EPSTEIN BARR VIRUS, HERPESVIRUS (1466)
 - FOCUS FORMATION, HUMAN SARCOMAS IN VITRO (1427)
 - GASTROINTESTINAL MALIGNANCIES, HUMAN FETAL GUT ANTIGEN (1566)
 - GROSS VIRUS, MURINE LEUKEMIA (1523)
 - GROUP-SPECIFIC, MURINE SARCOMA VIRUS (1476)
 - HEPATITIS-ASSOCIATED, FAMILIAL HEPATOMA (1712)*
 - LEUKEMIA, ASCITES TUMOR (1549)
 - LYMPHOBLASTOID CELLS, BURKITT'S LYMPHOMA, EPSTEIN BARR VIRUS (1532)
 - LYMPHOCYTES, MALIGNANT LYMPHOMA (1542)
 - MAREK'S DISEASE, HERPESVIRUS, PATHO-GENICITY (1467)
 - NEUROBLASTOMA, FETUS, ADRENALS (1577)
 - SENSITIZED MICE, SERUM PROTEIN CONCENTRATIONS, PRECANCEROUS CHANGES (1587)
 - STIMULATION, LYMPHOMA DEVELOPMENT, IMMUNOSUPPRESSIVE TREATMENT (1539)
 - SURFACE, FRIEND VIRUS, RAT TUMOR (1533)
 - SV40, TRANSFORMED HAMSTER CELLS (1525)
 - T, AMINO ACID COMPOSITION, ADENOVIRUS TYPE 12, HAMSTER (1526)
 - TRANSFORMED CELLS, SV40, UV-IRRADIATED (1537)
 - TSTA, ADENOVIRUS TYPE-12, MOUSE (1456)
 - TUMOR, INHIBITION OF MIGRATION, MACROPHAGE MIGRATION (1554)
 - TUMOR, SV40, KIDNEY CELLS (1538)
 - TUMOR COMPLEMENT FIXING, POLYOMA VIRUS (1510)
 - VIRAL, LOCALIZATION, IMMUNOFERRITIN, HERPES SIMPLEX (1521)
- AROMATIC HYDROCARBON
 - HEMOPATHY, HUMANS, OCCUPATIONAL HAZARD (1370)
 - MICROSOMES, CYTOCHROME PI-450, RAT (1344)
 - PETROLEUM ASPHALTS, COAL-TAR PITCH, SKIN TUMORIGENESIS (1330)
- ARSENIC
 - EPITHELIOMA, BOWEN'S DISEASE, HUMANS (1368)
- ASBESTOS
 - BRONCHIAL CANCER, PLEURAL MESOTHELIOMA (1610)
- ASCITES
 - ANTIGEN, LEUKEMIA (1549)
 - EHRlich TUMOR CELLS, UROPORPHYRIN (1702)
 - PERITONEAL FLUID, HEPATOMA, IMMUNITY (1555)

TUMOR, DNA, ORTHOPHOSPHATE, THYMIDINE,
LIVER (1648)
TUMOR, N-NITROSOBUTYLUREA, MYELOGENOUS
GRANULOCYTIC LEUKEMIA (1353)
TUMOR, TRANSFER OF PROTEINS TO
NUCLEOLUS, MOUSE (1658)
AZIRIDINE ETHANOL
SARCOMA INDUCTION, PROPANE SULFONE
(1291)
BENZENE
OCCUPATIONAL EXPOSURE, LEUKEMIA
INCIDENCE, ATOMIC BOMB IRRADIATION
(1399)
TOLUENE, OCCUPATIONAL HAZARD, ALKALINE
PHOSPHATASE, LEUKOCYTE LEVELS
(1374)*
BENZO(A)PYRENE
FIBROSARCOMA, EMBRYO, HAMSTER (1331)
HUMAN ORGANS, AGE, CARCINOGEN (1333)
METABOLISM OF CARCINOGEN, PRETREATMENT
WITH HYDROCARBONS (1335)
METABOLITES IN RAT BILE (1334)
PREGNANT MICE, PULMONARY ADENOMAS IN
PROGENY (1332)
P-BENZOQUINONE
INHALATION, MOUSE BRONCHIAL CELLS,
MALIGNANT CHANGES (1336)
BILE DUCT
CANCER, CHRONIC ULCERATIVE COLITIS
(1708)*
GENETIC SUSCEPTIBILITY, SPONTANEOUS
CHOLANGIOMA, MICE (1695)
HEPATOBIILIARY TRACT, TUMOR, INCIDENCE,
SOUTHERN ITALY (1630)*
BLADDER
2-ACETYLAMINOFLUORENE, 4-ETHYL-
SULFONYLNAPHTHALENE-1-SULFONAMIDE,
MOUSE, EPITHELIUM (1300)
CARCINOMA, ESTABLISHED CELL LINES,
EPITHELIAL, N-2-FLUORENYLACETAMIDE
(1304)
CARCINOMA, LYMPHOCYTE INFILTRATION
(1579)
N-2-FLUORENYLACETAMIDE DIET, CYCLO-
PHOSPHAMIDE (1302)
BLOOD
GROUPS, TUMOR INCIDENCE, PHENOTYPE,
REVIEW (1284)*
MALIGNANCIES, LIVER CARCINOMA, MYCO-
TOXINS (1276)
NEOPLASMS, METASTASES, MODEL (1681)
RETINOBLASTOMA, MALIGNANT CELLS
(1666)
BONE
OSTEOBLASTIC SARCOMA, OSSIFYING
FIBROMA, MICE, ALKALINE PHOSPHATASE
(1382)
OSTEOGENIC SARCOMA, IRRADIATION,
MANDIBULAR FIBROUS DYSPLASIA (1408)*
OSTEOSARCOMA, STRONTIUM 90, RAT
(1410)*
OSTEOSARCOMA, TIBIAL ENCHONDROMA
(1707)*
RADIUM KINETICS, THOROTRAST, MODEL,
RABBIT (1403)*
BONE MARROW
FACTOR, THYMIC DNA SYNTHESIS STIMULA-

TORY FACTOR (1657)
HEMATOPOIESIS, THYMUS, SPLEEN, RADIO-
STRONTIUM (1379)
OSTEOSARCOMA, STRONTIUM -90 (1381)
RECONSTITUTION, X-IRRADIATION,
IMMUNOLOGIC COMPETENCE, MICE (1594)
BRAIN
FIBROSARCOMAS, MONSTROCELLULAR
SARCOMAS, METHYLCHOLANTHRENE (1342)
MALIGNANT INFILTRATION, CELLULAR BLUE
NEVUS (1698)
MENINGIOMA, HYPERDIPLOIDY, CHROMOSOME,
HUMAN (1692)
BURKITT'S LYMPHOMA
CYCLOPHOSPHAMIDE, CHROMOSOMAL ABERRA-
TION (1364)
EPSTEIN BARR VIRUS (1432)
FEMALE TUMOR KARYOTYPE (1697)
ITALIAN CASE (1699)
LYMPHOBLASTOID CELLS, COMPLEMENT-
FIXING ANTIGENS, EPSTEIN BARR VIRUS
(1532)
CARBOHYDRATE
METABOLISM, CHICK LIVER, AFLATOXIN B1
(1311)
CARBON TETRACHLORIDE
HEPATOCAARCINOGENESIS, CREATIVE KINASE,
MOUSE (1288)
CARCINOGENICITY
AFLATOXIN B1, STRUCTURE-ACTIVITY
RELATIONSHIP (1308)
SEVIN, MANEB, CIRAM, CINEB, RAT
(1290)
CARCINOMA
ACHALASIA, ESOPHAGUS (1700)
MODEL, LUNG CELLS, CHINESE HAMSTER
(1675)
CELL
CARCINOGENIC, HYBRIDIZATION, HAMSTER
(1715)*
CULTURE, MITOTIC RATE, MOLONEY VIRUS,
ANTIGEN (1473)
EPIDERMAL, NEUTRON IRRADIATION, MOUSE
(1409)*
EPITHELIAL CELLS, URINARY BLADDER
CARCINOMA, N-2-FLUORENYLACETAMIDE
(1304)
HYBRIDS, SV40 PRODUCTION, UV RADIATION
IN VITRO (1517)*
NEW LINES, CANCER VIRUS, SV40, KIDNEY,
HUMAN SERUM (1501)
SENSITIVITY TO VIRAL INFECTION,
MOLONEY LEUKEMIA VIRUS, JLSV-9 CELLS
(1445)
SURFACE PROPERTIES, OCULAR MELANOMA,
ULTRASTRUCTURE (1670)
CERVIX
CARCINOMA, FIBROBLASTS, SKIN (1562)
CARCINOMA, KIDNEY TRANSPLANT, IMMUNO-
SUPPRESSION (1582)*
CARCINOMA, RECTUM, RADIATION THERAPY
(1395)
CERVICAL NEOPLASTIC CHANGE, RESERVE
CELL HYPERPLASIA, INCOMPLETE
SQUAMOUS METAPLASIA (1585)
7,12-DIMETHYLBENZ(A)ANTHRACENE,

* indicates a plain citation without accompanying abstract

CARCINOMA (1323)
HISTOCHEMICAL CHANGES, MALIGNANT
TRANSITION (1595)
MALIGNANT PROGRESSION, CYTOLOGICAL
SCREENING (1620)
VAGINA, DIETHYLSTILBESTROL, EPITHELIUM
(1294)
CHEMICAL CARCINOGEN
DIMETHYLNITROSAMINE, BACTERIAL
SYNTHESIS (1346)
FOOD ADDITIVES, PESTICIDES, ENVIRON-
MENTAL HUMAN CANCER (1275)
NATURALLY OCCURRING, SYMPOSIUM REVIEW
(1285)*
VIRUS PRODUCTION BY INFECTED CELLS,
X-IRRADIATION (1424)
CHEMOTACTIC AGENT
CANCER CELL FACTOR, MIGRATION,
INVASION (1682)
CHILDHOOD
THYMIC IRRADIATION, TUMORS (1396)
CHILDREN
ACUTE LYMPHOCYTIC LEUKEMIA,
EPIDEMIOLOGY (1603)
CANCER, LEUKEMIA, X-IRRADIATION
(1605)
CONGENITAL ANIRIDIA, HAMARTOMA,
SIMULTANEOUS OCCURRENCE WITH WILMS'
TUMOR (1709)*
FATHER AND SON OCCURRENCE, COLORECTAL
CARCINOMA (1696)
CHLORAMBUCIL
MYELOMONOCYTIC LEUKEMIA, CHRONIC
LYMPHOCYTIC LEUKEMIA (1365)
CHLORAMPHENICOL
MEDULLAR APLASIA, ACUTE LEUKEMIA, CASE
REPORT (1375)*
RAT HEPATOCARCINOGENESIS, 3'-METHYL-
4-DIMETHYLAMINOAZOBENZENE (1316)
CHLOROMA
PEROXIDASE ACTIVITY, RAT (1650)
CHOLESTEROL
GALLBLADDER, CARCINOMA, DIMETHYL-
NITROSAMINE, HAMSTER (1347)
3-METHYLCHOLANTHRENE, LECITHIN (1338)
SERUM, PARENTAL CANCER MORTALITY,
EPIDEMIOLOGY (1625)
CHROMATIN
PROTEINS, NA₂CO₃-EXTRACTABLE, 3-METHYL-
CHOLANTHRENE, RAT LIVER (1337)
CHROMOSOME
ABERRATION, CYCLOPHOSPHAMIDE BURKITT'S
LYMPHOMA CELLS (1364)
ABNORMALITIES, HUMAN LEUKEMIA,
INCREASED ERYTHROID MITOSES (1686)
ABNORMALLY LARGE, COLCHICINE,
WALDENSTROM'S MACROGLOBULINEMIA
(1688)
ANOMALIES, CHRONIC MYELOID LEUKEMIA,
PHILADELPHIA (1280)
ANOMALIES, NEPHROBLASTOMA, INFANTS,
KARYOTYPE (1685)
ANOMALY, PLASMOCYTIC LEUKEMIA, CASE
REPORT (1713)*
DNA, ASCITES, HEPATOMAS (1691)
FEMALE TUMOR KARYOTYPE, BURKITT'S
LYMPHOMA (U697)
HYPERDIPLOIDY, MENINGIOMAS, HUMAN
(1692)
KARYOTYPE, LYMPHOBLASTOID CELLS IN
VITRO, ACUTE LEUKEMIA (1693)
LUNG, SV40, HAMSTER (1498)
METAPHASE ABERRATIONS, HAMSTER LIVER
CELLS, COBALT 60 (1394)
METAPHASE DEFECTS, L-CYSTEINE,
PROTECTIVE ACTION (1360)
MISSING G GROUP, ATYPICAL KARYOTYPE,
CHRONIC MYELOGENOUS LEUKEMIA (1690)
MURINE SARCOMA -180, L-5178Y LYMPHO-
BLAST (1661)
NEUROBLASTS, X-IRRADIATION, DNA
SYNTHESIS (1391)
NORMAL, MEDULLARY THYROID CARCINOMA
(1710)*
PH1-LIKE, FAMILIAL TRANSMISSION
(1719)*
PHILADELPHIA, Y, MYELOID LEUKEMIA,
CASE REPORT (1721)*
THIOACETAMIDE, LIVER (1297)
TRANSLOCATION INDUCTION, MOUSE
SPERMATOGONIA, X-IRRADIATION (1392)
VIRUS, BOVINE KIDNEY CELLS, HAMSTER
LUNG CELLS (1491)
COLCHICINE
WALDENSTROM'S MACROGLOBULINEMIA,
ABNORMALLY LARGE CHROMOSOME (1688)
COLON
STOMACH, ARGYROPHIL CELLS, NEOPLASIA
(1590)
CROWN GALL
TERATOMA, GLUTAMINE (1694)
CYCLOPHOSPHAMIDE
BLADDER CARCINOMAS, N-2-FLUORENYL-
ACETAMIDE DIET (1302)
BURKITT'S LYMPHOMA CELLS, CHROMOSOMAL
ABERRATION (1364)
CYTOGENETICS
3-METHYLCHOLANTHRENE, MOUSE MAMMARY
CARCINOMA (1340)
CYTOTOXICITY
SERUM FRACTION ANTIBODIES, GROUP
SPECIFIC ANTIGENS, RAUSCHER VIRUS,
MOUSE (1448)
DIBUTYLNITROSAMINE
SYRIAN AND CHINESE HAMSTERS, CARCINOMA
DEVELOPMENT (1351)
DIET
POLYUNSATURATED FAT-RICH DIET,
CARCINOMA MORTALITY (1363)
DIETHYLNITROSAMINE
LIVER, CYCLOHEXIMIDE, RAT (1372)*
MICE, TUMOR TYPES, ORGAN SUSCEPTI-
BILITY (1348)
PAPILLOMAS, TRACHEAL MUCOSA,
HAMSTERS, NUCLEIC ACID (1349)
PULMONARY CARCINOGENESIS, GOLDEN
HAMSTER, ORGANOTROPY (1345)
DIETHYLSTILBESTROL
CERVIX, VAGINA, EPITHELIUM (1294)
NEPHROBLASTOMA, ULTRASTRUCTURE
HAMSTER (1373)*
DIFFERENTIATION

MALIGNANT, BENIGN, SQUAMOUS CELL
 CARCINOMA, RAT (1588)
 N,N-DIMETHYL-4-AMINOAZOBENZENE
 DAB-REDUCTASE, RAT LIVER (1315)
 4-DIMETHYLAMINOAZOBENZENE
 IMMUNE RAT LYMPH NODES, HEPATOMA
 (1550)
 P-DIMETHYLAMINOAZOBENZENE
 LIVER, SYNESTROL, TESTOSTERONE, RAT
 (1314)
 PHOSPHOFRUCTOKINASE, LIVER, RAT
 (1318)
 PREGNENOLONE, LIVER CANCERIZATION,
 RATS, HYPOTHALAMUS (1313)
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 BUCCAL POUCH, EPIDERMAL CARCINOMA,
 ANTILYMPHOCYTE SERUM (1541)
 CARCINOMA, CERVIX (1323)
 EMBRYO, DNA, RNA, ACTINOMYCIN D,
 1-MERCAPTO-1-(BETA-4-PYRIDETHYL)
 BENZIMIDAZOLE (1322)
 FIBROSARCOMA, EMBRYO, HAMSTER (1331)
 GUINEA PIGS, CONTACT SENSITIVITY
 (1324)
 MELANOID TUMORS, GOLDEN HAMSTER,
 PINEALECTOMY, SEX DIFFERENCE (1328)
 PAPILLOMA, PHORBOL ESTER ACETATE
 (1321)
 PHAGOCYTOSIS, ANTIBODY, LEUKEMIA,
 LIVER (1451)
 PREGNANT MICE, PULMONARY ADENOMA IN
 PROGENY (1332)
 RAUSCHER LEUKEMIA VIRUS, CELL TRANS-
 FORMATION (U326)
 SQUAMOUS CARCINOMAS, ANTITHYMOCYTE
 SERUM (1325)
 SYNESTROL, OSTEOSARCOMA, RABBIT
 (1329)
 TUMOR REGRESSION, OVARIECTOMY (1327)
 VIRUS, HERPES SIMPLEX VIRUS, VIRUS
 INFECTIVITY (1463)
 DIMETHYLNITROSAMINE
 CARCINOMA, GALLBLADDER, CHOLESTEROL,
 HAMSTER (1347)
 DIMETHYLAMINE, SODIUM NITRITE,
 BACTERIAL SYNTHESIS, RAT INTESTINE
 (1346)
 MICE, TUMOR TYPES, ORGAN SUSCEPTIBIL-
 ITY (1348)
 DNA
 ASCITES, HEPATOMAS, CHROMOSOMES (1691)
 LEUKEMIA, MITOCHONDRIAL, FLOTATION
 DENSITY, REVIEW (1270)
 LIVER, ASCITES TUMOR, ORTHOPHOSPHATE,
 THYMIDINE (1648)
 MALIGNANT FIBROBLASTS, CELL CULTURE,
 MOUSE (1717)*
 MAMMARY CARCINOMA, COLLAGENASE,
 NITROGEN, INVASION (1649)
 4-NITROQUINOLINE-1-OXIDE, NUCLEOSIDE,
 ELECTRON SPIN RESONANCE (1355)
 REPAIR, ULTRAVIOLET RADIATION,
 XERODERMA PIGMENTOSUM (1388)
 REPAIR SYNTHESIS, VIRUS (1356)
 REPLICATION, N-HYDROXY-2-ACETYLAMINO-
 FLUORENE, BINDING (1298)

REPLICATION, VIRUS, SV40, CYCLO-
 HEXIMIDE (1504)
 SARCOMA -180, PROLIFERATION KINETICS
 (1627)
 SINGLE-STRANDED, DOUBLE-STRANDED,
 SYNTHESIS, MURINE LEUKEMIA VIRUS
 (1446)
 SKIN, SQUAMOUS CELL EPITHELIOMA,
 CYTOPHOTOMETRY (1722)*
 SV40, ETHIDIUM BROMIDE, STRUCTURE
 (1494)
 SV40, KIDNEY, BSC-1 CELLS, PROPERTIES
 (1492)
 SV40, UPTAKE, DEAE DEXTRAN (1502)
 SYNTHESIS, INDUCTION, SV40 (1499)
 SYNTHESIS, NEUROBLASTS, X-IRRADIATION
 (1391)
 SYNTHESIS, POLYOMA VIRUS, MITOCHONDRIA
 (1513)
 SYNTHESIS, RNA DEPENDENT, ONCOGENESIS,
 NORMAL CELL DEVELOPMENT (1268)
 SYNTHESIS, THYMIC STIMULATORY FACTOR,
 BONE MARROW (1657)
 SYNTHESIS, X-RAY, KIDNEY, EHRLICH
 CELLS, LIVER (1390)
 TEMPERATURE SENSITIVE MUTANT, ADENO-
 VIRUS 31 (1458)
 TUMOR, FEULGEN CYTOPHOTOMETRY, BENIGN,
 MALIGNANT, HUMAN (1640)
 VIRAL FORMS, CYCLOHEXIMIDE, SV40
 (1503)

EMBRYO

7,12-DIMETHYLBENZ(A)ANTHRACENE, DNA,
 RNA, ACTINOMYCIN D, 1-MERCAPTO-1-
 (BETA-4-PYRIDETHYL)BENZIMIDAZOLE
 (1322)
 IMPLANTATION, ULTRASTRUCTURE OF TERA-
 TOMAS, MURINE TERATOMAS (1671)

ENDOMETRIUM

CARCINOMA, HYPERPLASIA (1282)
 HYPERPLASIA, INTRAUTERINE DEVICE
 (1706)

ENVIRONMENTAL FACTOR

CANCER, EPIDEMIOLOGY, ITALY (1622)
 CYTOCHROME P1-450, POLYCYCLIC HYDRO-
 CARBONS, MICROSOMES, RAT (1344)
 HUMAN CANCER, FOOD ADDITIVES, PESTI-
 CIDES (1275)
 NATURAL CARCINOGENS, SYMPOSIUM REVIEW
 (1285)*
 NEOPLASMS IN AQUATIC ANIMALS, BOTTOM
 FEEDING FISH, OYSTERS, COMPARATIVE
 ONCOLOGY (1273)

ENZYME

ACID PHOSPHATASE, MOUSE, CEREBRUM,
 ASCITES (1684)
 ACID PHOSPHATASE ISOENZYME, RETICULUM
 CELLS, LEUKEMIC RETICULOENDOTHELIO-
 SIS (1637)
 ADENOSINE DEAMINASE ACTIVITY, PLATE-
 LETS, CHRONIC MYELOID LEUKEMIA
 (1643)
 ALKALINE PHOSPHATASE, LEUKOCYTES,
 BENZENE, TOLUENE, OCCUPATIONAL
 HAZARD (1374)*
 AMINOPEPTIDASE ACTIVITY, MOUSE MAMMAR

TUMOR VIRUS (1470)
 ARGINASE, SV40, FIBROSARCOMA, LIVER, HAMSTER (1496)
 L-ASPARAGINASE, ANTIBODY, ASCITIC LEUKEMIA (1560)
 L-ASPARAGINASE, INHIBITION OF FOCUS-FORMATION, ROUS SARCOMA VIRUS, METHOTREXATE (1480)
 L-ASPARAGINASE, MITOTIC ACTIVITY IN LIVER CELLS, N-2-FLUORENYLACETAMIDE (1303)
 COLLAGENASE, CARCINOGENESIS, SKIN, MICE, DNA (1343)
 COLLAGENASE, MAMMARY CARCINOMA, INVASION ZONE, DNA (1649)
 CREATINE KINASE, CARBON TETRACHLORIDE, HEPATOCARCINOGENESIS, MOUSE (1288)
 DAB-REDUCTASE, N,N-DIMETHYL-4-AMINO-AZOBENZENE, RAT LIVER (1315)
 DIHYDROFOLATE REDUCTASE, LYMPHOMA L1210 (1646)
 DNA POLYMERASE, RNA DEPENDENT, MOLONEY LEUKEMIA VIRUS, STREPTOVARICIN (1444)
 ESTERASE ACTIVITY, PLASMA, IRRADIATION RATS (1387)
 GLUCOSE-6-PHOSPHATE DEHYDROGENASE, A AND B TYPES, MULTIPLE CELL ORIGIN OF TUMOR, HEREDITARY NEUROFIBROMA (1687)
 GLYCOLYSIS, OXIDATIVE, SV40, SIMIAN KIDNEY CELLS (1506)
 INDUCTION, BENZO(A)PYRENE, METABOLISM OF CARCINOGEN (1335)
 ISOCITRATE DEHYDROGENASE, LACTATE DEHYDROGENASE, LYMPHOBLASTIC LEUKEMIA, SPLEEN, LIVER, BURSA (1644)
 LACTATE DEHYDROGENASE, LEUKEMIA, VIRUS INTERFERON (1454)
 LACTATE DEHYDROGENASE ISOENZYMES, PROSTATIC CANCER, SV40, HUMAN, HAMSTER (1508)
 LYSOSOMAL, LIVER AND KIDNEY TISSUE, RENAL CARCINOMA (1645)
 LYSOSOMAL CHANGES, LIVER, METASTASES, NONIONIC SURFACTANTS (1680)
 PEROXIDASE ACTIVITY, CHLOROMA, RAT (1650)
 PHOSPHOFRUCTOKINASE, P-DIMETHYLAMINO-AZOBENZENE, RAT LIVER (1318)
 SUCCINIC DEHYDROGENASE, CYTOCHEMISTRY, AFLATOXIN B1, MUCOR HIEMALIS FUNGUS (1376)*
 THYMIDINE KINASE, YABA VIRUS, TUMORS (1429)
 EPIDEMIOLOGY
 ACUTE LYMPHOCYTIC LEUKEMIA, CHILDHOOD LEUKEMIA (1603)
 AMERICAN NEGROES, INCIDENCE OF BRONCHOGENIC CANCER (1623)
 CANCER, CONNECTICUT, CIGARETTE SMOKING (1611)
 CANCER, ENVIRONMENTAL FACTORS, BERGAMO ITALY (1622)
 CANCER, SUBSAHARAL AFRICA (1608)
 CANCER MORTALITY, REGIONAL TEMPERATURE VARIATION (1617)
 CANCER MORTALITY, STATISTICAL COMPILATION, UNITED STATES (1602)
 CONNECTICUT, LIP CANCER (1612)
 DIAGNOSIS, MALIGNANT MELANOMA (1632)*
 ENGLISH CHILDREN, AFRICAN CHILDREN, HODGKIN'S DISEASE (1607)
 JEWISH POPULATION, POLYCYTHEMIA VERA, INCREASED RISK OF MALIGNANCY (1615)
 LYMPHOGRANULOMATOSIS, POLAND (1629)*
 MICROEPIDEMICS, VIRAL ONCOGENESIS IN MAN (1267)
 MULTIPLE PRIMARY TUMORS, MAMMARY CANCER, FEMALE REPRODUCTIVE ORGANS (1621)
 NEW MEXICO INDIANS, BILE DUCT CANCER, GALLBLADDER CANCER (1616)
 NONAFRICAN UGANDANS, AFRICAN UGANDANS, TUMOR INCIDENCE (1609)
 PARENTAL CANCER MORTALITY, SERUM CHOLESTEROL AMONG OFFSPRING (1625)
 TUMOR, QUEBEC (1631)*
 TUMOR, SMOKING, TUNISIA (1628)*
 UNITED STATES, OVARIAN CANCER, UTERINE CANCER (1619)
 UTAH, SURVIVAL RATE, MELANOMA (1614)
 WEST GERMAN ARMY, LEUKEMIA (1613)
 EPITHELIOMA
 ARSENIC, BOWEN'S DISEASE, HUMANS (1368)
 ERYTHROCYTE
 ROLE, PHYTOHEMAGGLUTININ-STIMULATED HUMAN LYMPHOCYTES (1571)
 ESOPHAGUS
 ACHALASIA, CARCINOMA, HUMAN (1700)
 ESTROGEN
 MAMMARY CARCINOGENESIS, X-IRRADIATION (1295)
 ETHIONINE
 NODULES, LIVER, ULTRASTRUCTURE (1296)
 4-ETHYLSULFONYLNAPHTHALENE-1-SULFONAMIDE
 MOUSE, BLADDER, EPITHELIUM (1300)
 EWING'S TUMOR
 ORIGIN OF TUMOR, GROWTH PATTERN OF TUMOR IN VITRO (1704)
 EYE
 RETINOBLASTOMA, BLOOD (1666)
 FEMUR
 MEDULLARY CANAL, 90S GAMMA, 90Y, DOSIMETRY, RAT (1405)*
 FIBROBLAST
 DIFFUSION CHAMBER, SPONTANEOUS MALIGNANT TRANSFORMATION, MURINE (1584)
 LIVER, VIRUS PARTICLES (1413)
 LUNG, SV40, SUSCEPTIBILITY (1490)
 RIBOSOMAL RNA, ACTINOMYCIN D (1659)
 VIRUS TRANSFORMED, DENSITY INHIBITION, MOUSE (1500)
 FIBROSARCOMA
 SMALLPOX VACCINATION (1416)
 N-2-FLUORENYLACETAMIDE
 L-ASPARAGINASE, MITOTIC ACTIVITY IN LIVER CELLS (1303)
 CYCLOPHOSPHAMIDE, BLADDER CARCINOMAS (1302)
 CYCLOPHOSPHAMIDE, ESTABLISHED CELL

LINES, URINARY BLADDER CARCINOMA (1304)
 LIVER CARCINOGENESIS, HYPERPLASTIC HEPATIC NODULES (1299)
 LIVER PLASMA MEMBRANES, LIPID COMPOSITION (1305)
 POLYNUCLEOTIDE, FLUORENYLAMINE, RNA, DNA (1306)
 1,1-BIS(4-FLUOROPHENYL)-2-PROPYNYL N-CYCLOHEPTYLCARBAMATE
 MALIGNANT LYMPHOMA, RAT (1287)
 1,1-BIS(4-FLUOROPHENYL)-2-PROPYNYL N-CYCLOOCTYLCARBAMATE
 MALIGNANT LYMPHOMA, RAT (1287)
 FOLIC ACID
 CARCINOGENIC METAL CHELATES (1292)
 FREUND ADJUVANT
 BERGOLZ VIRUS, RETICULOSARCOMATOSIS, MOUSE (1477)
 THYMUS, LUNGS, CELL PROLIFERATION, GUINEA PIG (1307)
 GALLBLADDER
 CANCER, NEW MEXICO INDIANS, BILE DUCT (1616)
 CARCINOMA, CHOLESTEROL, DIMETHYL-NITROSAMINE, HAMSTER (1347)
 GASTROINTESTINAL TRACT
 HUMAN FETAL GUT ANTIGEN, MALIGNANCIES, DETECTION OF ANTIGEN (1566)
 SCHWANN CELLS, NEURINOMA, PATHOGENESIS FIBROCYTES (1593)
 GENETICS
 AUTOSOMAL DOMINANT INHERITANCE, CONGENITAL CANCER, REVIEW (1278)
 CONGENITAL TUMOR, IMMUNITY, ACTIVE, ADOPTIVE (1547)
 FORWARD MUTATIONS, 8-AZAGUANINE SENSITIVITY, X-IRRADIATION (1393)
 HEREDITARY NEUROFIBROMA, DOUBLE ENZYME PHENOTYPE, MULTIPLE CELL ORIGIN OF TUMOR (1687)
 MOSAICISM, OVARIAN TUMOR, GONADOBLASTOMA (1689)
 PARENTAL CANCER MORTALITY, EPIDEMIOLOGY, SERUM CHOLESTEROL (1625)
 SOLID TUMOR, LEUKEMIA, INCIDENCE IN TWINS, MORTALITY (1606)
 VIRAL GENOME, ROUS SARCOMA VIRUS, HAMSTER CELLS (1486)
 WHITE-NEGRO ADMIXTURE, BREAST CANCER INCIDENCE (1699)
 GLIOMA
 BRAIN, PROTEIN S100 (1567)
 CANINE, ULTRASTRUCTURE, ROUS SARCOMA VIRUS (1484)
 GROWTH
 ASCITIC LEUKEMIA, L-ASPARAGINASE, ANTIBODY (1560)
 CARCINOGENESIS, NORMAL CELL DEVELOPMENT, RNA DEPENDENT DNA SYNTHESIS (1268)
 CARCINOMA, SKIN, CERVIX, NASOPHARYNX (1562)
 CELL CYCLE, HUMAN LEUKEMIA, TUMOR GROWTH KINETICS (1281)
 INVASIVE TUMORS, ACID PHOSPHATASE,

MOUSE, CEREBRUM (1684)
 LIVER, PARTIAL HEPATECTOMY, RATS (1350)
 PATTERN OF TUMOR IN VITRO, EWING'S TUMOR, ORIGIN (1704)
 RATE, PAROTID GLAND TUMOR, 32P ACCUMULATION (1634)*
 RATE, TUMOR, RISK, BRONCHOGENIC CARCINOMA (1626)
 REGULATION, CELL, PROTEIN CONFORMATION, SERUM (1673)
 TRANSFORMED CELLS, SV40, HERPES SIMPLEX (1493)
 TUMOR, PROMOTION, SODIUM COBALTNITRIDE, COBALT CHLORIDE (1339)
 TUMOR VASCULARIZATION, TUMOR ANGIOGENESIS FACTOR (1647)
 HEMATOPOIESIS
 GAMMA-RAY, NEUTRON IRRADIATION (1380)
 HEPATOMA
 ASCITES, PERITONEAL FLUID, IMMUNITY, PASSIVE TRANSFER (1555)
 ALPHA-FETOPROTEIN, ISOLATION, HUMAN (1580)*
 HISTOCHEMISTRY
 ADRENALS, WHOLE BODY IRRADIATION, RAT (1407)*
 HISTOGENESIS
 TRANSPLANT, MAMMARY GLAND, ISOGRAFT (1665)
 HISTOLOGY
 RECTAL MUCOSA, EARLY CARCINOMA (1599)
 HISTOPATHOLOGY
 TUMOR, CHICK-EMBRYO-LETHAL-ORPHAN ADENOVIRUS (1459)
 HODGKIN'S DISEASE
 CONCURRENT LIVER CARCINOMA (1718)*
 EPSTEIN BARR VIRUS, VIRAL ANTIBODY TITERS (1434)
 INCIDENCE, ENGLISH CHILDREN, AFRICAN CHILDREN (1607)
 LYMPHOCYTES, PROLIFERATION KINETICS, PHYTOHEMAGGLUTININ (1720)*
 HORMONE
 CHORIONIC GONADOTROPIN, RADIATION, ANDREOBLASTOMA (1594)
 ECTOPIC PRODUCTION, HUMAN CHORIONIC SOMATOMAMMOTROPIN, NONTROPHOBLASTIC CANCERS (1656)
 SYNESTROL, 7,12-DIMETHYLBENZ(A)ANTHRACENE, OSTEOSARCOMA, RABBIT (1329)
 SYNESTROL, KIDNEY TUMORS, MORPHOGENESIS, HAMSTER (1586)
 SYNTHESIS, TROPHOBLASTIC TUMOR CELLS, HUMAN CHORIOCARCINOMA (1653)
 THYROCALCITONIN, MEDULLARY CARCINOMA, THYROID, URINE (1638)
 TUMOR REGRESSION, OVARIECTOMY, 7,12-DIMETHYLBENZ(A)ANTHRACENE (1327)
 HUMAN CHORIONIC SOMATOMAMMOTROPIN, NONTROPHOBLASTIC CANCERS, ECTOPIC PRODUCTION OF HORMONE (1656)
 HYBRIDIZATION
 CARCINOGENICITY, HAMSTER (1715)*
 MURINE SARCOMA -180, L-5178Y LYMPHOBLAST, CHROMOSOME (1661)

* indicates a plain citation without accompanying abstract

N-HYDROXY-2-ACETYLAMINOFLUORENE
 BINDING TO DNA, REPLICATION (1298)
 4-HYDROXYAMINOQUINOLINE
 MONOACETYL, SARCOMA INDUCTION IN MICE
 (1359)
 4-HYDROXYAMINOQUINOLINE-1-OXIDE
 METABOLISM, LIVER, BLOOD, MICE (1358)
 HYPERPLASIA
 ENDOMETRIAL CARCINOMA (1282)
 FAMILIAL ADENOMATOSIS, ENDOCRINE,
 WERNER'S DISEASE, SURGERY, REVIEW
 (1279)
 RESERVE CELL, INCOMPLETE SQUAMOUS
 METAPLASIA, CERVICAL NEOPLASTIC
 CHANGE (1585)
 IATROGENIC TUMOR
 ANTICONVULSANT CHEMOTHERAPY,
 OVARIAN THECOMA (1371)
 IMMUNITY
 ACTIVE, CONGENITAL TUMOR, ADOPTIVE
 IMMUNITY, MOUSE (1547)
 ALLOGRAFTS, ANTILYMPHOCYTE SERUM,
 LYMPHOID CELLS, MICE (1559)
 ASCITES, PERITONEAL FLUID, PASSIVE
 TRANSFER (1555)
 AUTOCHTHONOUS TUMOR CELLS, LYMPHOCYTE
 RESPONSE, HUMAN (1574)
 CELLULAR AND HUMORAL IMMUNE RESPONSE,
 GROSS VIRUS LYMPHOMA (1531)
 COMPETENCE, LYMPHOID CELLS,
 X-IRRADIATION (1544)
 DEFECTIVE IMMUNE RESPONSE, SPLEEN,
 RIDGEWAY SARCOMA IN MICE (1548)
 FRIEND LEUKEMIA VIRUS, MACROPHAGE
 MIGRATION (1534)
 HUMAN TUMORS, INHIBITORY FACTOR,
 LEUCOCYTE MIGRATION (1545)
 INHIBITION OF MIGRATION, TUMOR
 ANTIGENS, MACROPHAGE (1554)
 PATHOLOGY OF VIRAL INFECTIONS, MURINE
 SARCOMA VIRUS (1472)
 SIMIAN ADENOVIRUS POPULATION,
 HUMAN ADENOVIRUS POPULATION (1457)
 SKIN GRAFTS, LYMPHOSARCOMA, MICE
 (1558)
 TUMOR SURVIVAL TIME, YEAST RNA, MICE
 (1556)
 TUMOR TRANSPLANTATION, 6-METHYL-
 CHOLANTHRENE, INHIBITION OF IMMUNE
 RESPONSE (1551)
 IMMUNIZATION
 CYTOLYTIC POTENCY, MOUSE LEUKEMIA
 ANTISERA, RABBIT (1553)
 IMMUNOGLOBULIN
 CARBOHYDRATE, BIOSYNTHESIS, MOUSE
 PLASMA CELL TUMOR (1565)
 IGG3, MOUSE SERUM, MURINE MYELOMA
 (1568)
 MURINE PLASMACYTOMA, CELL CULTURE OF
 TUMOR (1546)
 IMMUNOLOGY
 ADENOVIRUS TYPE 12, TUMOR, MOUSE
 (1456)
 CONTACT SENSITIVITY, 7,12-DIMETHYL-
 BENZ(A)ANTHRACENE, GUINEA PIGS
 (1324)
 ENHANCEMENT OF TUMOR ISOGRAFT, RNA
 FROM TUMOR-IMMUNIZED ANIMALS (1561)
 IMMUNO-ACCELERATOR, LENTINAN (1583)*
 MAREK'S DISEASE, HERPESVIRUS, VIRUS
 (1468)
 PREGNANT MOTHERS, OFFSPRING IMMUNITY,
 LEUKEMIA, GROSS VIRUS (1449)
 ROUS SARCOMA VIRUS, ANTIGEN COMPLEX,
 CHICK CELLS (1527)
 SERUM FRACTIONS, RAUSCHER VIRUS, MOUSE
 (1448)
 THYMUS, NEOPLASIA, REVIEW (1272)
 TUMOR INCIDENCE, PHENOTYPE, BLOOD
 GROUPS, REVIEW (1284)*
 IMMUNOSUPPRESSION
 ADENOCARCINOMA, THYMECTOMY, RADIATION,
 MICE (1552)
 ANTIGENIC STIMULATION, LYMPHOMA
 DEVELOPMENT (1539)
 ANTILYMPHOCYTE SERUM, 3-METHYLCHOL-
 ANTHRENE, MICE (1540)
 ANTITHYMOCYTE SERUM, SQUAMOUS
 CARCINOMAS, DMBA (1325)
 KIDNEY TRANSPLANT, CERVICAL CARCINOMA
 (1582)*
 MAMMARY TUMOR VIRUS, ALLOGRAFT
 SURVIVAL (1530)
 MOUSE SPLEEN, FRIEND LEUKEMIA VIRUS
 (1529)
 MURINE LEUKEMIA TRANSPLANT, NORMAL
 TISSUE RNA (1557)
 ORGAN TRANSPLANT, LYMPHOMAGENESIS,
 ANTIGEN STIMULATION (1589)
 INFECTIOUS MONONUCLEOSIS
 ACUTE LYMPHOCYTIC LEUKEMIA, EPSTEIN
 BARR VIRUS (1578)
 INFECTIVITY
 DIFFERENTIAL, VIRAL SEROLOGICAL TYPE,
 HERPESVIRUS HOMINIS (1460)
 VIRUS, HETEROGENEITY, AVIAN ERYTHRO-
 BLASTOSIS (1437)
 INFILTRATION
 MALIGNANT, CELLULAR BLUE NEVUS, BRAIN
 (1698)
 INHIBITOR
 FACTOR, LEUCOCYTE MIGRATION, HUMAN
 TUMORS (1545)
 LENTINAN, IMMUNO-ACCELERATOR (1583)*
 INTERFERON
 FIBROBLASTS, LEUKEMIA, SARCOMA, VIRUS
 (1528)
 INDUCTION, HAMSTER, POLYOMA VIRUS
 (1519)
 LEUKEMIA, VIRUS, LACTATE DEHYDROGENASE
 (1454)
 INTESTINE
 CAPILLARIES, GAMMA RAY IRRADIATION,
 FRACTIONATED DOSE (1383)
 CHRONIC ULCERATIVE COLITIS, BILIARY
 TRACT CANCER (1708)*
 COLON AND RECTUM, JUVENILE POLYP
 (1591)
 COLORECTAL CARCINOMA, FATHER AND SON
 OCCURRENCE (1696)
 INTRACISTERNAL VIRAL PARTICLES
 MURINE LEUKEMIC TISSUES, VIRUS (1442)
 INTRAUTERINE CONTRACEPTIVE DEVICE

ENDOMETRIAL HYPERPLASIA (1706)

IODINE
THYROID, PARATHYROID, NEOPLASTIC
HUMAN (1635)

ISOPROTERENOL
MOUSE KIDNEY CELLS, PROLIFERATION
(1674)

KIDNEY
CELLS C-TYPE VIRUS PARTICLES, PIG
(1428)
DNA, SV40, BSC-1 CELLS (1492)
NEPHROBLASTOMA, CHROMOSOMES, INFANTS,
KARYOTYPE (1685)
NEPHROBLASTOMA, DIETHYLSTILBESTROL,
HAMSTER (1373)*
RENAL CARCINOMA, LYSOSOMAL ENZYME
ACTIVITY, LIVER (1645)
RENAL TUMORS, CLEAR CELL, RATS (1352)
RNA VIRUS, CHICKS, AVIARY MYELOBLAS-
TOMA (1436)
THOROTRAST, HUMANS (1404)*
TUMOR, RENAL PELVIS, CORAL CALCULUS,
PATHOGENESIS (1600)*

LEUKEMIA
ACUTE, KARYOTYPE STUDIES, LYMPHO-
BLASTOID CELLS IN VITRO (1693)
ACUTE, MEDULAR APLASIA, CHLORAMPHENI-
COL, CASE REPORT (1375)*
ACUTE LYMPHOCYTIC, EPIDEMIOLOGY,
CHILDREN (1603)
ACUTE LYMPHOCYTIC, EPSTEIN BARR VIRUS,
INFECTIOUS MONONUCLEOSIS (1578)
ACUTE LYMPHOCYTIC, MALIGNANT LYMPHOMA,
HERPESVIRUS SAIMIRI (1464)
ANTIGEN, ASCITES (1549)
ANTISERA, IMMUNE REACTION IN RABBIT,
CYTOLYTIC POTENCY (1553)
ASCITIC, L-ASPARAGINASE, ANTIBODY
(1560)
CELL CYCLE, TUMOR GROWTH KINETICS,
HUMAN (1281)
CHILDHOOD, EXPOSURE TO CATS (1604)
CHRONIC MYELOGENOUS, ATYPICAL KARYO-
TYPE, MISSING G GROUP CHROMOSOME
(1690)
CHRONIC MYELOID, PLATELETS, ADENOSINE
DEAMINASE ACTIVITY (1643)
CLOSTRIDIA, IMMUNOSUPPRESSION, REVIEW
(1286)*
FRIEND VIRUS, SPLEEN PARABIOSIS (1453)
GASTRIC AND LUNG CANCER, VIRUS-LIKE
PARTICLES, VIRUS (1414)
HUMAN, LEUKOCYTIC LEUKEMIA VIRUS,
MORPHOLOGY (1418)
INCIDENCE, JAPAN, ATOMIC BOMB
SURVIVORS (1398)
INCIDENCE IN WEST GERMAN ARMY (1613)
INCREASED ERYTHROID MITOSES, CHROMO-
SOME ABNORMALITIES, HUMAN (1686)
INTERFERON, POLYINOSINIC-POLYCYTIDYLIC
ACID, FIBROBLASTS (1528)
LYMPHOBLASTIC, LACTATE DEHYDROGENASE,
ISOCITRATE DEHYDROGENASE, LIVER,
SPLEEN, BURSA (1644)
LYMPHOCYTIC, ANTILYMPHOCYTE SERUM,
MURINE VIRUS (1543)

LYMPHOID, BENZENE, OCCUPATIONAL HAZARD
(1370)
MOLONEY VIRUS, C-TYPE PARTICLES (1447)
MURINE, GROSS VIRUS, ANTIGEN (1523)
MURINE LEUKEMIC TISSUES, INTRACISTER-
NAL VIRAL PARTICLES (1442)
MYELOGENOUS, MULTIPLE MYELOMA, EPSTEIN
BARR VIRUS, CELL SURFACE (1433)
MYELOGENOUS GRANULOCYTIC, N-NITRO-
SOBURYUREA, ASCITES TUMOR (1353)
MYELOID, CHROMOSOME ANOMALIES,
CHRONIC, ACUTE, PHILADELPHIA CHROMO-
SOME (1280)
MYELOID, PHILADELPHIA CHROMOSOME,
Y CHROMOSOME, CASE REPORT (1721)*
MYELOMONOCYTIC, CHRONIC LYMPHOCYTIC,
CHLORAMBUCIL (1365)
NUCLEIC ACIDS, RNA, DNA (1431)
OCCUPATIONAL EXPOSURE TO BENZENE,
ATOMIC BOMB IRRADIATION (1399)
PLASMOCYTIC, CHROMOSOMAL ANOMALIES,
CASE REPORT (1713)*
RNA, DNA, SYNTHESIS, POLYMERASE (1641)
SARCOMA, RADIONUCLIDES, REVIEW (1274)
SOLID TUMOR, MORTALITY, INCIDENCE IN
TWINS (1606)
TRANSPLANT, NORMAL TISSUE RNA, IMMUNO-
SUPPRESSION, MOUSE (1557)
X-IRRADIATION, CHILDHOOD CANCER (1605)

LEUKOCYTE
HUMAN, METAPHASE DEFECTS, L-CYSTEINE,
PROTECTIVE ACTION (1360)
MIGRATION INHIBITOR, HUMAN TUMORS,
IMMUNITY (1545)

LIP
CANCER, INCIDENCE IN CONNECTICUT
(1612)

LIPID
CARCINOMA MORTALITY, POLYUNSATURATED
FAT-RICH DIET (1363)
COMPOSITION, N-2-FLUORENYLACETAMIDE,
LIVER PLASMA MEMBRANES (1305)
ESSENTIAL FATTY ACIDS, WHOLE BLOOD,
EHRlich ASCITES CARCINOMA,
SARCOMA 180 (1655)
FATTY TISSUE, MAMMARY TUMOR, SURFACE
MOTILITY, PHAGOCYTOSIS (1679)
LECITHIN, CHOLESTEROL, 3-METHYL-
CHOLANTHRENE (1338)

LIVER
2-ACETYLAMINOFLUORENE, METABOLITE
BINDING, NUCLEIC ACIDS, RAT (1301)
ANTIBODY, PHAGOCYTOSIS, LEUKEMIA,
SPLEEN, 7,12-DIMETHYLBENZ(A)ANTHRA-
CENE (1451)
BINDING, ORTHO-AMINOAZOTOLUENE,
REGENERATION (1320)
BLOOD, LUNG, 4-HYDROXYAMINOQUINOLINE-
1-OXIDE (1358)
CANCER, STEROIDS, RATS, LEYDIG CELLS,
HYPOTHALAMUS (1313)
CARBOHYDRATE METABOLISM, AFLATOXIN B1,
CHICK (1311)
CARCINOMA, BLOOD MALIGNANCIES, MYCO-
TOXINS (1276)
CARCINOMA, HODGKIN'S DISEASE (1718)*
CELL PROLIFERATION, RATS, HOMEOSTATIC

* indicates a plain citation without accompanying abstract

- REGULATION (1350)
- CELLS, METAPHASE CHROMOSOME ABERRATIONS, COBALT 60, HAMSTER (1394)
- CHROMATIN PROTEINS, 3-METHYLCHOLANTHRENE, NA C1-EXTRACTABLE, RAT (1337)
- CHROMOSOMES, THIOACETAMIDE (1297)
- CIRRHOSIS, TUMOR, PATHOGENESIS (1598)*
- CREATINE KINASE, CARBON TETRACHLORIDE, CARCINOGENESIS, MOUSE (1288)
- DIETHYLNITROSAMINE, CYCLOHEXIMIDE, RAT (1372)*
- P-DIMETHYLAMINOAZOBENZENE, SYNESTROL, TESTOSTERONE, RAT (1314)
- DNA, ASCITES TUMOR, ORTHOPHOSPHATE, THYMIDINE (1648)
- ETHIONINE NODULES, ULTRASTRUCTURES, RAT (1296)
- FAMILIAL HEPATOMA, HEPATITIS-ASSOCIATED ANTIGEN (1712)*
- N-2-FLUORENYLACETAMIDE, HYPERPLASTIC HEPATIC NODULES (1299)
- GAMMA RADIATION, ALPHA-AMINOISOBUTYRIC ACID, RAT (1386)
- HAMSTER FIBROSARCOMA, SV40, ARGINASE (1496)
- HEPATOCARCINOGENESIS, 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE, CHLORAMPHENICOL, RAT (1316)
- HEPATOCAINOMA, SENEIO LONGILOBUS (1293)
- HEPATOMA, COLONY INHIBITION, IMMUNE LYMPH NODES, RAT (1550)
- HEPATOMA, DNA, CHROMOSOMES (1691)
- HEPATOMA, ETHANOLAMINE, CHOLINE (1660)
- HEPATOMA, MITOCHONDRIAL MEMBRANE PROTEINS, RAT (1652)
- HEPATOMA, RNA, SUBRIBOSOMAL PARTICLES (1636)
- IN VITRO MALIGNANT TRANSFORMATION, AFLATOXIN B1, RAT (1312)
- LYSOSOMAL ENZYME ACTIVITY, RENAL CARCINOMA (1645)
- MICROSOME, FOWL, REPTILE, AFLATOXIN B1 METABOLISM (1309)
- OLEIC ACID, LINOLEIC ACID, STEARIC ACID, MALIGNANT NEOPLASMS (1639)
- PHOSPHOFRUCTOKINASE, P-DIMETHYLAMINO-AZOBENZENE, RAT (1318)
- PLASMA MEMBRANES, LIPID COMPOSITION, N-2-FLUORENYLACETAMIDE (1305)
- THOROTRAST, CIRRHOSIS, CARCINOMA, HUMAN (1397)
- TUMOR, 3'-METHYL-4-DIMETHYLAMINO-AZOBENZENE, SOLUBLE MACROMOLECULES, RAT (1317)
- VIRUS PARTICLES, FIBROBLASTS (1413)
- AMYLOID DEPOSITS, OAT-CELL CARCINOMA, MORPHOLOGY (1664)
- BENZO(A)PYRENE, PREGNANT MICE, PROGENY, PULMONARY ADENOMA (1332)
- BRONCHIAL CANCER, PLEURAL MESOTHELIOMA ASBESTOS EXPOSURE (1610)
- BRONCHOGENIC CARCINOMA, TUMOR GROWTH, RISK (1628)
- CANCER, GOLDEN HAMSTERS, DIETHYL-NITROSAMINE, ORGANOTROPY (1345)
- CANCER, PATHOGENESIS, ETIOLOGY, TOBACCO (1597)
- CANCER, SKIN CANCER, OCCUPATIONAL HAZARD (1277)
- CELLS, CARCINOMA, 3H-THYMIDINE, CHINESE HAMSTER (1675)
- CHROMOSOMES, SV40, HAMSTER (1498)
- FIBROBLASTS, SV40 (1490)
- INCIDENCE OF BRONCHOGENIC CANCER, AMERICAN NEGROES (1623)
- MOUSE BRONCHIAL CELLS, MALIGNANT CHANGES, PARA-BENZOQUINONE INHALATION (1336)
- OVINE PULMONARY ADENOMAS, ULTRASTRUCTURE OF TUMORS, VIRAL PARTICLES (1411)
- PULMONARY CARCINOMA, MICE, CIGARETTE SMOKE (1367)
- SQUAMOUS EPITHELIAL CARCINOMA, STRUCTURAL CHANGES, BRONCHOGENIC (1662)
- THORIUM 232, CIGARETTE SMOKERS (1400)
- TRAUMA, CARCINOMA, PATHOGENESIS (1406)*
- LYMPH NODE
- IMMUNE, COLONY INHIBITION, RAT HEPATOMA (1550)
- LYMPHATICS
- MOLONEY LEUKEMIA VIRUS VARIANT, TUMORIGENESIS IN MICE, VIRUS (1443)
- LYMPHOBLAST
- ACUTE LEUKEMIA, KARYOTYPE STUDIES (1693)
- HUMAN LYMPHOBLASTOID CELL LINES, EPSTEIN BARR VIRUS (1435)
- LYMPHOCYTE
- ANTILYMPHOCYTE SERUM, LEUKEMIA, MURINE VIRUS (1543)
- INFILTRATION, URINARY BLADDER CARCINOMA (1579)
- LYMPHOID CELLS, ALLOGRAFTS, ANTI-LYMPHOCYTE SERUM, MICE (1559)
- MONONUCLEAR CELLS, PHYTOHEMAGGLUTININ-P, PERITONEAL FLUID (1572)
- PROLIFERATION KINETICS, HODGKIN'S DISEASE, LYMPHADENOSIS, PHYTOHEMAGGLUTININ (1720)*
- PUROMYCIN, ACTINOMYCIN D, PHYTOHEMAGGLUTININ (1678)
- RESPONSE, HUMAN, AUTOCHTHONOUS TUMOR CELLS (1574)
- RESPONSE, PHYTOHEMAGGLUTININ, DOWN'S SYNDROME (1570)
- LYMPHOGRANULOMATOSIS
- EPIDEMIOLOGY, POLAND (1629)*
- LYMPHOMA
- ANTIGENIC STIMULATION, IMMUNOSUPPRESSIVE TREATMENT (1539)
- CELLULAR AND HUMORAL IMMUNE RESPONSE, GROSS VIRUS (1531)
- CYTOTOXIC ANTIBODY RESPONSE, GROSS LEUKEMIA VIRUS (1520)
- HERPESVIRUS SAIMIRI, ACUTE LYMPHOCYTIC LEUKEMIA (1464)
- L1210, DIHYDROFOLATE REDUCTASE (1646)

MALIGNANT, LYMPHOCYTES, ANTIGENS
(1542)
ORGAN TRANSPLANTS, IMMUNOSUPPRESSION,
ANTIGEN, HYPERPLASIA (1589)
LYMPHOPROLIFERATIVE DISEASE
WALDENSTROM'S MACROGLOBULINEMIA,
ABNORMALLY LARGE CHROMOSOME,
COLCHICINE (1688)
LYMPHOSARCOMA
SKIN GRAFTS, MICE (1558)
MACROPHAGE
INHIBITION OF MIGRATION, TUMOR ANTIGEN
(1554)
MIGRATION, FRIEND LEUKEMIA VIRUS,

IMMUNITY (1534)
MAMMARY GLAND
BREAST CANCER INCIDENCE, WHITE-NEGRO
GENETIC ADMIXTURE (1699)
CARCINOGENESIS, ESTROGEN TREATMENT,
X-IRRADIATION (1295)
CARCINOMA, COLLAGENASE, DNA, NITROGEN,
INVASION (1649)
CARCINOMA, LEUKOCYTES, VIRUS, LUNG
(1420)
CARCINOMA, 3-METHYLCHOLANTHRENE,
KARYOTYPE, MOUSE (1340)
CARCINOMA, WEIGHT, AGE AT FIRST
PREGNANCY (1618)
FATTY TISSUE, SURFACE MOTILITY, CELLS
(1679)
FEMALE REPRODUCTIVE ORGANS, MULTIPLE
PRIMARY TUMORS (1621)
FIBROADENOMAS, ADOLESCENTS (1705)
MULTIPLE FIBROADENOMAS, HORMONAL
CONTRACEPTIVES (1378)*
PROLACTIN, MITOTIC ACTIVITY, RAT
(1676)
TRANSPLANT HISTOGENESIS, ISOGRAFT
(1665)
TUMOR INCIDENCE, MAMMARY TUMOR VIRUS,
MOUSE INBRED STRAINS (1471)
TUMOR VIRUS, AMINOPEPTIDASE ACTIVITY
(1470)
TUMOR VIRUS, HUMAN MILK (1419)
MAREK'S DISEASE
HERPESVIRUS, IMMUNE RESPONSE IN
CHICKENS (1468)

MELANIN
CARCINOGENESIS, REVIEW (1283)*

MELANOMA
INCIDENCE IN UTAH, SURVIVAL RATE
(1614)
MALIGNANT, DIAGNOSIS, EPIDEMIOLOGY
(1632)*
OCULAR, ULTRASTRUCTURE, SURFACE
PROPERTIES (1670)

MEMBRANE
CELLULAR TRANSMEMBRANE ELECTRICAL
POTENTIAL, MITOSIS, MALIGNANT CELLS
(1677)
PHOSPHOLIPIDS, HEPATOMA CELLS,
CALCIUM, MAGNESIUM (1651)
PROTEINS, MITOCHONDRIA, LIVER,
HEPATOMA, RAT (1652)
SMOOTH, ROUGH, MYELOMA, MOUSE (1667)
MENINGEOMA

HYPERDIPLOIDY, CHROMOSOMES, HUMAN
(1692)
METABOLISM

BENZO(A)PYRENE, PRETREATMENT, INDUC-
TION, RAT BILE (1334)
EHRlich ASCITES CARCINOMA,
SARCOMA 180, ESSENTIAL FATTY ACIDS,
WHOLE BLOOD (1655)
ENERGY EXPENDITURE, WALKER TUMOR, RAT
(1703)
GLIOBLASTOMA, LACTATE PRODUCTION,
TUMOR REGIONAL HISTOCHEMISTRY, MOUSE
(1698)
MALIGNANT NEOPLASMS, LIVER, OLEIC
ACID, LINOLEIC ACID, STEARIC ACID
(1639)

METAL
CARCINOGENIC METAL CHELATES, FOLIC
ACID (1292)
COBALT CHLORIDE, SODIUM COBALTNITRIDE
PROMOTION OF TUMOR GROWTH (1339)

METASTASIS
HAMSTER TUMORS, LYSOSOMAL CHANGES,
LIVER, NONIONIC SURFACTANTS (1680)
MIGRATION OF TUMOR CELLS, INVASION,
CHEMOTACTIC CANCER CELL FACTOR
(1682)
NEOPLASMS, BLOODBORNE, MODEL (1681)
SPREAD OF INOCULATED TUMOR CELLS,
WALKER 256 TUMOR, ULTRASTRUCTURE
(1683)

METHOTREXATE
ROUS SARCOMA VIRUS, L-ASPARAGINASE,
INHIBITION OF FOCUS-FORMATION (1480)
METHYLCHOLANTHRENE
FIBROSARCOMAS, MONSTROCELLULAR SARCOMA
(1342)

3-METHYLCHOLANTHRENE
ANTILYMPHOCYTE SERUM, MICE, IMMUNO-
SUPPRESSION (1540)
CARCINOGEN BINDING IN RAT LIVER
(1341)
CARCINOGENESIS, MICE, SKIN, DNA,
COLLAGENASE (1343)
CHROMATIN PROTEINS, NAcl EXTRACTABLE,
RAT LIVER (1337)
CYTOGENETICS, MOUSE MAMMARY CARCINOMA
(1340)
LECITHIN, CHOLESTEROL (1338)
TUMOR TRANSPLANTATION, INHIBITION OF
IMMUNE RESPONSE (1551)
3'-METHYL-4-DIMETHYLAMINOAZOBENZENE
CHLORAMPHENICOL, RAT HEPATOCARCINO-
GENESIS (1316)
SOLUBLE MACROMOLECULES, RAT LIVER
TUMORS (1317)
N-METHYL-N'-NITRO-N-NITROSOGUANIDINE
MOUSE GASTRIC CYSTS, LEIOMYOSARCOMA
(1354)

MICROORGANISM
CLOSTRIDIA, IMMUNOSUPPRESSION,
CARCINOGENESIS, LEUKEMIA, REVIEW
(1286)*

MICROSOME
POLYCYCLIC HYDROCARBONS, CYTOCHROME
P1-450, ENVIRONMENT, RAT (1344)

* indicates a plain citation without accompanying abstract

MITOCHONDRIA
DNA, TOPOGRAPHY, LEUKEMIA, FLOTATION DENSITY (1270)
DNA SYNTHESIS, POLYOMA VIRUS (1513)
MEMBRANE PROTEIN, LIVER, HEPATOMA, RAT (1652)

MITOSIS
CELL CULTURES, MORPHOLOGY, MOLONEY VIRUS, ANTIGEN (1473)
LIVER CELLS, N-2-FLUORENYLACETAMIDE, L-ASPARAGINASE (1303)
MALIGNANT CELLS, CELLULAR TRANS-MEMBRANE ELECTRICAL POTENTIAL (1677)
PROLACTIN, RAT MAMMARY GLAND (1676)
SODIUM, DNA SYNTHESIS, TRANSMEMBRANE POTENTIAL, ONCOGENESIS (1269)

MORPHOLOGY
THYMUS, CANCER AT VARIOUS SITES, REVIEW (1271)

MYELOMA
IMMUNOGLOBULIN IGG3, MOUSE SERUM (1568)
GAMMA 1-IMMUNOGLOBULIN, HEAVY CHAIN, PRIMARY STRUCTURE (1581)*
MULTIPLE, ANTIBODIES, KEYHOLE LIMPET HEMOCYANIN (1576)
PROTEINS, HEAVY CHAIN MUTANTS, MOUSE (1564)
SMOOTH MEMBRANES, ROUGH MEMBRANES, MOUSE (1667)

2-NAPHTHYL N-METHYLCARBAMATE
BETA-SEVIN, CARCINOGENICITY, RAT, MOUSE (1289)

NASOPHARYNX
CARCINOMA, HUMAN, UNCLASSIFIED VIRUS (1423)
CERVIX, SKIN, FIBROBLASTS, CARCINOMA (1562)

NERVE
SEVERANCE, TUMORIGENESIS, COCKROACH, TUMOR TRANSMISSION (1701)

NEURINOMA
GASTROINTESTINAL TRACT, RECKLINGHAUSEN DISEASE, SCHWANN CELLS, PATHOGENESIS (1593)

NEUROBLASTOMA
ANTIGENS, FETUS, ADRENALS (1577)

ULTRASTRUCTURE, ANNULATE LAMELLAE, HUMAN (1684)

NEUROMA
TRAUMA, ULTRASTRUCTURE (1402)*

NEVUS
CELLULAR BLUE, MALIGNANT INFILTRATION, OF BRAIN (1698)
-NITROQUINOLINE-1-OXIDE
DNA, NUCLEOSIDES, ELECTRON SPIN RESONANCE (1355)
SARCOMA, MICE (1357)
VIRUS, DNA REPAIR SYNTHESIS (1356)
-NITROSOBUTYLUREA
ASCITES TUMOR, MYELOGENOUS GRANULOCYTIC LEUKEMIA (1353)

NUCLEIC ACID
2-ACETYLAMINOFLUORENE, METABOLITE BINDING (1301)
DNA SYNTHESIS, RNA, LEUKEMIA (1641)

EMBRYO, ACTINOMYCIN D, 7,12-DIMETHYLBENZ(A)ANTHRACENE, 1-MERCAPTO-1-(BETA-4-PYRIDETHYL)BENZIMIDAZOLE (1322)
FLUORENYLAMINE POLYNUCLEOTIDE, RNA, DNA, 2-FLUORENYLHYDROZYLAMINE (1306)
PROTEIN SYNTHESIS, VIRUS (1426)
RNA, DNA, SYNTHESIS, LEUKEMIA (1431)
SYNTHESIS, BINDING, ORTHO-AMINO-AZOTOLUENE, MOUSE LIVER (1320)
TRACHEAL PAPILLOMA, HAMSTERS, DIETHYL-NITROSAMINE (1349)
URETHAN, PROTEIN, INTERACTION (1362)

NUCLEOTIDE
ETHANOLAMINE, CHOLINE, HEPATOMA, RAT (1660)

NUCLEUS
NUCLEAR BODIES, MALIGNANT TUMORS, BENIGN TUMORS, ELECTRON MICROSCOPY (1672)

OCCUPATIONAL HAZARD
BENZENE, TOLUENE, LEUKEMIA (1370)
RESPIRATORY CANCER, STEELWORKERS, COKE WORKERS, MORTALITY RATES (1369)
SKIN CANCER, RESPIRATORY CANCER (1277)
TOLUENE, BENZENE, ALKALINE PHOSPHATASE, LEUKOCYTE LEVEL (1374)*

ORAL CAVITY
BUCCAL POUCH, EPIDERMOID CARCINOMA, ANTILYMPHOCYTE SERUM, 7,12-DIMETHYLBENZ(A)ANTHRACENE (1541)
CARCINOMA, INDIA, TOBACCO (1624)

ORAL CONTRACEPTIVE
MULTIPLE MAMMARY FIBROADENOMAS (1378)*

ORGAN TRANSPLANTATION
LYMPHORETICULAR NEOPLASM, IMMUNOSUPPRESSION, ANTIGEN, HYPERPLASIA (1589)

ORTHOAMINOAZOTOLUENE
BINDING, LIVER CELLS, NUCLEIC ACID SYNTHESIS (1320)

OSTEOSARCOMA
BONE MARROW, STRONTIUM -90 (1381)
7,12-DIMETHYLBENZ(A)ANTHRACENE, SYNESTROL, RABBIT (1329)

OVARY
CANCER, UNITED STATES INCIDENCE, UTERINE CANCER (1619)
OVARIECTOMY, TUMOR REGRESSION, 7,12-DIMETHYLBENZ(A)ANTHRACENE (1327)
RADIATION EXPOSURE, CHORIONIC GONADOTROPIN, ANDREOBLASTOMA (1594)
RAT CORPORA LUTEA, STEROIDOGENESIS, ANILINE (1319)
THECOMA, ANTICONVULSANT CHEMOTHERAPY (1371)
TUMORS, GENETIC MOSAICISM, GONADOBLASTOMA (1689)

PAPILLOMA
PHORBOL ESTER ACETATE, 7,12-DIMETHYLBENZ(A)ANTHRACENE (1321)

PARATHYROID
ADENOMA, ULTRASTRUCTURE, CILIA (1669)
THYROID, HUMAN, IODINE, HUMAN (1635)

PAROTID GLAND

TUMOR, GROWTH RATE, 32P ACCUMULATION (1634)*

PATHOGENESIS
CARCINOMA OF RECTUM, MUCOSAL FOLDS, PERILESIONAL CHANGES (1592)
KIDNEY TUMOR, SYNESTROL, HAMSTER (1586)
TUMOR, RENAL PELVIS, CORAL CALCULUS (1600)*

PATHOLOGY
IMMUNOGENICITY, MURINE SARCOMA VIRUS (1472)

PERIODATE
INDUCTION OF LYMPHOCYTE TRANSFORMATION (1377)*

PESTICIDES
ENVIRONMENTAL HUMAN CANCER, FOOD ADDITIVES (1275)
SEVIN, MANEB, CIRAM, CINEB, CARCINOGENICITY, RAT (1290)

PETS
DOMESTIC CATS, CHILDHOOD LEUKEMIA, EXPOSURE (1604)
FELINE LYMPHOMA, VIRUS, SARCOMA (1441)

PHLEOMYCIN
POLYOMA, VIRUS SYNTHESIS IN VITRO (1511)

PHORBOL
ESTER ACETATE, PAPILLOMA, 7,12-DIMETHYLBENZ(A)ANTHRACENE (1321)

PHOSPHOLIPID
HEPATOMA CELLS, CALCIUM, MAGNESIUM, MEMBRANE (1651)
SYNTHESIS, POLYOMA VIRUS, HAMSTER CELLS (1514)

PHYTOHEMAGGLUTININ
HUMAN LYMPHOCYTES, ROLE OF ERYTHROCYTE (1571)
LYMPHOCYTE RESPONSE, DOWN'S SYNDROME (1570)
LYMPHOCYTES, PROLIFERATION, LYMPHADENOSIS, LYMPHOGRANULOMATOSIS (1720)*
P, MONONUCLEAR CELLS, PERITONEAL FLUID (1572)
THYMUS, MICE (1573)

PINEAL BODY
MELANOID TUMORS, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, GOLDEN HAMSTERS, SEX (1328)

PLACENTA
ANEMIA-INDUCING SUBSTANCE, MUCOPROTEIN IN URINE OF CANCER PATIENTS, COMMON ANTIGENICITY (1575)
HUMAN CHORIOCARCINOMA, TROPHOBLASTIC TUMOR CELLS, HORMONE SYNTHESIS (1653)

PLANT
SENECIO LONGILOBUS, HEPATOCARCINOMA (1293)

PLASMA
CELL TUMOR, IMMUNOGLOBULIN, CARBOHYDRATE, BIOSYNTHESIS, MOUSE (1565)
LEUKEMIC PLATELETS, CHRONIC MYELOID LEUKEMIA, ADENOSINE DEAMINASE ACTIVITY (1643)

PLASMACYTOMA
CELL CULTURE OF TUMOR, IMMUNOGLOBULIN PRODUCTION, MURINE (1546)

POLYCYTHEMIA
VERA, JEWISH POPULATION, INCREASED RISK OF MALIGNANCY (1615)

POLYPS
JUVENILE, COLON AND RECTUM (1591)

PRECANCEROUS CONDITION
MALIGNANT TRANSITION, CERVIX UTERI, HISTOCHEMICAL CHANGES (1595)
SERUM PROTEIN CONCENTRATIONS, ANTIGEN-SENSITIZED MICE (1587)
UTERUS, SEX CHROMATIN, CYTOLOGY, HUMAND (1596)

PROLACTIN
RAT MAMMARY GLAND, MITOTIC ACTIVITY (1676)

PROLIFERATION
FREUND'S ADJUVANT, GUINEA PIG, THYMUS (1307)
KINETICS, DNA, SARCOMA -180 (1627)
MOUSE KIDNEY CELLS, ISOPROTERENOL (1674)
TUMOR GROWTH KINETICS, HUMAN LEUKEMIA, TUMOR CELLS (1281)

PROPANE SULTONE
AZIRIDINE ETHANOL, SARCOMA INDUCTION (1291)

PROSTATE
CANCER, HAMSTER, HUMAN, VIRUS, LACTATE DEHYDROGENASE ISOENZYMES (1508)
CARCINOMA, SV40, PROGESTOGEN TREATMENT (1505)

PROTEIN
ALPHA-FETOPROTEIN, ISOLATION, HEPATOMA, HUMAN (1580)*
CARCINOGEN BINDING IN RAT LIVER, 3-METHYLCHOLANTHRENE (1341)
CONFORMATION, CELL GROWTH REGULATION, SERUM (1673)
GAMMA1-IMMUNOGLOBULIN, HEAVY CHAIN, PRIMARY STRUCTURE, MYELOMA (1581)*
GROUP-SPECIFIC, CANCER PATIENTS (1569)
MUCOPROTEIN, URINE OF CANCER PATIENTS
ANEMIA-INDUCING PLACENTAL SUBSTANCE
COMMON ANTIGENICITY (1575)
MYELOMA, HEAVY CHAIN MUTANTS, MOUSE (1564)
PLASMA, IRRADIATION, RATS, ESTERASE ACTIVITY (1387)
ROUS SARCOMA VIRUS, STRUCTURAL (1482)
S100, BRAIN GLIOMAS (1567)
STRUCTURAL, HERPES SIMPLEX VIRUS (1462)
SYNTHESIS, NUCLEIC ACIDS, PAPOVA VIRUS (1426)
TRANSFER OF PROTEINS TO NUCLEOLUS, MOUSE ASCITES TUMOR (1658)

RADIATION
ATOMIC BOMB, BENZENE, OCCUPATIONAL EXPOSURE, LEUKEMIA INCIDENCE (1399)
ATOMIC BOMB SURVIVORS, JAPAN, INCIDENCE OF LEUKEMIA (1398)
CARCINOMA, CERVICAL, RECTAL (1395)
COBALT 60, METAPHASE CHROMOSOME

* indicates a plain citation without accompanying abstract

ABERRATIONS, HAMSTER LIVER CELLS (1394)
 EPIDERMAL CHANGES, 10B(N,ALPHA)7LI REACTION, SWINE (1384)
 FEMUR, 90S GAMMA, 90Y, DOSIMETRY, RAT (1405)*
 GAMMA RAY, INTESTINAL CAPILLARIES, FRACTIONATED DOSE (1383)
 GAMMA RAY, RAT LIVER, ALPHA-AMINO-ISOBUTYRIC ACID (1386)
 MANDIBULAR FIBROUS DYSPLASIA, OSTEOGENIC SARCOMA (1408)*
 NEUTRON, GAMMA RAY, HEMOPOIETIC CFU (1380)
 NEUTRON, MOUSE EPIDERMAL CELLS, CELL SURVIVAL (1409)*
 OSTEOSARCOMA, STRONTIUM 90, RAT (1410)*
 OVARY, CHORIONIC GONADOTROPIN, TUMOR DEVELOPMENT (1594)
 RADIONUCLIDES, LEUKEMIA, SARCOMA, REVIEW (1274)
 RADIUM 224, OSTEOBLASTIC SARCOMA, ALKALINE PHOSPHATASE, MICE (1382)
 RATS, ESTERASE, PLASMA (1387)
 SKIN, HEMANGIOMA, CASE REPORT (1401)*
 SKIN, NEUTRON BEAM, SWINE (1385)
 STRONTIUM, HAEMATOPOIESIS, SPLEEN, THYMUS, BONE MARROW (1379)
 STRONTIUM -90, OSTEOSARCOMA, BONE MARROW (1381)
 THORIUM 232, CIGARETTE SMOKERS, ACCUMULATION OF THORIUM IN LUNGS (1400)
 THOROTRAST, HUMAN LIVER, CIRRHOSIS, CARCINOMA (1397)
 THYMUS TUMORS, CHILDHOOD (1396)
 ULTRAVIOLET, FIBROBLASTS, XERODERMA PIGMENTOSUM (1388)
 ULTRAVIOLET, MURINE LEUKEMIA VIRUS, MURINE SARCOMA VIRUS, INACTIVATION (1452)
 ULTRAVIOLET, VIRUS, BRAIN (1489)
 ULTRAVIOLET INACTIVATION, ROUS SARCOMA VIRUS HELPER (1479)
 WHOLE BODY, ADRENAL GLAND, HISTOCHEMISTRY, RAT (1407)*
 X-RAY, CHEMICAL CARCINOGENS, VIRUS PRODUCTION BY INFECTED CELLS (1424)
 X-RAY, DNA SYNTHESIS, KIDNEY, EHRLICH CELLS, LIVER (1390)
 X-RAY, DNA SYNTHESIS, NEUROBLASTS (1391)
 X-RAY, ESTROGEN TREATMENT, MAMMARY CARCINOGENESIS (1295)
 X-RAY, FORWARD MUTATIONS, 8-AZAGUANINE SENSITIVITY (1393)
 X-RAY, LEUKEMIA, CHILDHOOD CANCER (1605)
 X-RAY, LYMPHOID CELLS, IMMUNOLOGIC COMPETENCE (1544)
 X-RAY, TRANSLOCATION INDUCTION, MOUSE SPERMATOGONIA (1392)
 KINETICS, BONE MARROW-FREE SKELETON,

THOROTRAST, MODEL, RABBIT (1403)*
 RECTUM
 CARCINOMA, EARLY STAGE, MUCOSA, HISTOLOGY (1599)*
 CARCINOMA, MUCOSAL FOLDS (1592)
 CARCINOMA, RADIATION THERAPY, CERVICAL CARCINOMA (1395)
 RESPIRATORY TRACT
 CANCER, COKE WORKERS, STEELWORKERS, MORTALITY RATES (1369)
 CIGARETTE SMOKE, HAMSTERS, SMOKE PARTICLE DEPOSIT, LUNGS (1366)
 RETICULOENDOTHELIOSIS
 LEUKEMIC, ACID PHOSPHATASE ISOENZYME, RETICULUM CELLS (1637)
 RETINOBLASTOMA
 BLOOD, MALIGNANT CELLS (1666)
 RNA
 DOUBLE STRANDED PENICILLIUM, REGRESSION OF SPLENOMEGALY, VIRUS, FRIEND LEUKEMIA VIRUS (1450)
 FELINE LEUKEMIA VIRUS (1440)
 LIVER, HEPATOMAS, SUBRIBSOMAL PARTICLES (1636)
 NORMAL TISSUE, MURINE LEUKEMIA TRANSPLANT, IMMUNOSUPPRESSION (1557)
 RIBOSOMAL, FIBROBLASTS, ACTINOMYCIN D (1659)
 TUMOR-IMMUNIZED ANIMALS, ENHANCEMENT OF TUMOR ISOGRAFT (1561)
 VIRAL, HYBRIDIZATION, DNA-POLYMERASE, CHICK LEUKEMIC VIRUS, BASE SEQUENCES (1438)
 VIRUS, MURINE MAMMARY TUMOR, FLUORESCENCE MICROSCOPY (1469)
 VIRUS-SPECIFIC, ROUS SARCOMA (1487)
 YEAST, TUMOR SURVIVAL TIME, IMMUNIZED MICE (1556)
 SALIVARY GLAND
 GARDNER'S SYNDROME (1601)*
 SARCOMA
 DEFECTIVE MOLONEY VIRUS, MAZURENKO VIRUS, MOUSE (1475)
 LEIOMYOSARCOMA, N-METHYL-N'-NITRO-NITROSOGUANIDINE, MOUSE GASTRIC CYST (1354)
 LEUKEMIA, RADIONUCLIDES, REVIEW (1274)
 MONOACETYL, 4-HYDROXYAMINOQUINOLINE, MICE (1359)
 4-NITROQUINOLINE-1-OXIDE, MICE (1357)
 180, DNA, PROLIFERATION KINETICS (1677)
 SCALP
 TONGUE, NEOPLASIA, MINERAL OIL, WALNUT SHELL DYE, MOROCCO (1633)*
 SERUM
 ANTILYMPHOCYTE, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, BUCCAL POUCH, EPIDERMAL CARCINOMA (1541)
 ANTILYMPHOCYTE, 3-METHYLCHOLANTHRENE, MICE, IMMUNOSUPPRESSION (1540)
 CANCER PATIENTS, GROUP-SPECIFIC PROTEIN CONCENTRATIONS (1569)
 PROTEIN, CELL GROWTH REGULATION, PROTEIN CONFORMATION (1673)
 PROTEIN CONCENTRATIONS, ANTIGEN-SENSITIZED MICE, PRECANCEROUS

CHANGES (1587)

SEX
CHROMATIN, UTERINE TUMOR CELLS,
CYTOLOGY, HUMANS (1596)

SKIN
CANCER, RESPIRATORY CANCER, OCCUPA-
TIONAL HAZARD (1277)
COLLAGENASE, CARCINOGENESIS, DNA,
MICE (1343)
EPIDERMAL CHANGES, 10B(N,ALPHA)7LI
REACTION RADIATION (1384)
EPIDERMAL PAPILLOMAS, SHOPE PAPILLOMA
VIRUS (1522)
EPIDERMIS, LARGE-CELL ACANTHOMAS
(1585)
EPITHELIOMA, BOWEN'S DISEASE, ARSENIC,
HUMANS (1368)
FIBROBLASTS, CARCINOMA, NASOPHARYNX,
CERVIX (1562)
HEMANGIOMA, RADIATION-INDUCED, CASE
REPORT (1401)*
RADIATION, NEUTRON BEAM, SWINE (1385)
SQUAMOUS CARCINOMAS, ANTITHYMOCYTE
SERUM, DMBA (1325)
SQUAMOUS CELL EPITHELIOMA, DNA,
CYTOPHOTOMETRY (1722)*
TUMORIGENESIS, COAL-TAR PITCH,
PETROLEUM ASPHALTS (1330)

SPLEEN
DEFECTIVE IMMUNE RESPONSE, RIDGEWAY
SARCOMA IN MICE (1548)
IMMUNOSUPPRESSION, FRIEND LEUKEMIA
VIRUS, MOUSE (1529)

LEUKEMIA, FRIEND VIRUS, PARABIOSIS
(1453)
REGRESSION OF SPLENOMEGALY, FRIEND
LEUKEMIA VIRUS, DOUBLE-STRANDED
PENICILLIUM RNA (1450)
ULTRASTRUCTURE OF ANTIBODY-FORMING
CELLS, FRIEND LEUKEMIA VIRUS, MOUSE
(1535)

SODIUM
ONCOGENESIS, DNA SYNTHESIS, MITOSIS
(1269)

STEROID
ADRENOCORTICAL VIRILIZING CARCINOMA
(1642)

STOMACH
ARGYROPHIL CELLS, NEOPLASIA, COLON
(1590)
CARCINOMA, GASTRIC SURGERY, PEPTIC
ULCER (1711)*
MOUSE GASTRIC CYSTS, LEIOMYOSARCOMA,
N-METHYL-N'-NITRO-N-NITROSOGUANIDINE
(1354)

SUBMAXILLARY GLAND
POLYOMA, VIRUS, CHROMOSOME (1512)

SURFACTANT
NONIONIC, LYSOSOMAL CHANGES, TUMOR
METASTASES (1680)

SUSCEPTIBILITY
GENETIC, LIVER BILE DUCTS, SPON-
TANEOUS CHOLANGIOMA, MICE (1695)
LONG-TERM CELL CULTURE, RAT, VIRUS
(1412)
SPECIES-SPECIFIC VIRUS, INFECTION OF

HUMAN-MOUSE HYBRID CELLS, VIRUS
(1507)

SYNDROME
GARDNER'S, TUMOR, MAXILLAR (1601)*

TEMPERATURE
VARIATION, EPIDEMIOLOGY, REGIONAL
CANCER MORTALITY (1617)

TERATOMA
CROWN GALL, GLUTAMINE (1694)
EMBRYO IMPLANTATION, ULTRASTRUCTURE,
MURINE (1671)

THIOACETAMIDE
LIVER, CHROMOSOMES (1297)

THOROTRAST
KIDNEY, HUMANS (1404)*
RADIUM KINETICS, BONE MARROW-FREE
SKELETON, MODEL, RABBIT (1403)*

THYMUS
ALTERATIONS, CANCER AT VARIOUS SITES,
REVIEW (1271)
CELL PROLIFERATION, FREUND'S ADJUVANT,
GUINEA PIG (1307)

CULTURE, RAT, MOLONEY LEUKEMIA VIRUS,
C PARTICLES (1447)
IMMUNE RESPONSE, CARCINOGENESIS,
REVIEW (1272)
IRRADIATION, TUMORS, CHILDHOOD (1396)
MICE, PHYTOHEMAGGLUTININ (1573)
RADIOSTRONTIUM, HAEMATOPOIESIS,
SPLEEN, BONE MARROW (1379)

THYROID
CARCINOMA, ULTRASTRUCTURE (1714)*
C-CELL ADENOMA, MEDULLARY CARCINOMA,
FLUOROGENIC AMINES (1654)
MEDULLARY CARCINOMA, NORMAL CHROMO-
SOMES (1710)*
NEOPLASTIC THYROID, IODINE, HUMAN
(1635)
URINE, THYROCALCITONIN, MEDULLARY
CARCINOMA (1638)

TOBACCO
CIGARETTE SMOKERS, ACCUMULATION OF
THORIUM IN LUNGS, THORIUM 232
(1400)
CIGARETTE SMOKING, CANCER INCIDENCE,
CONNECTICUT (1611)
CIGARETTES, MICE, PULMONARY CARCINOMA,
SEX (1367)
INDIA, ORAL CAVITY CARCINOMA (1624)
LUNG CANCER PATHOGENESIS, ETIOLOGY
(1597)
SMOKE, DEPOSITION, HAMSTERS, LUNGS,
RADIOACTIVITY (1366)

TONGUE
NEOPLASIA, MOROCCO, INCIDENCE, WALNUT
SHELL DYE (1633)*

TRACHEA
PAPILLOMA, NUCLEIC ACIDS, DIETHYL-
NITROSAMINE, HAMSTERS (1349)

TRANSFORMATION
IN VITRO, MALIGNANT, AFLATOXIN B1,
RAT LIVER (1312)
LYMPHOCYTE, PERIODITE (1377)*
RAT EMBRYO, 7,12-DIMETHYLBENZ(A)-
ANTHRACENE, RAUSCHER LEUKEMIA VIRUS
(1326)
ROUS SARCOMA VIRUS, HAMSTERS, IN VIVO

* indicates a plain citation without accompanying abet.

IN VITRO (1481)
 SPONTANEOUS MALIGNANT, MOUSE FIBRO-
 BLASTS, DIFFUSION CHAMBER (1584)
 VACCINE VIRUS, MOUSE EMBRYO CELLS
 (1415)
 TRANSMISSION
 TUMOR, NERVE SEVERANCE TUMORIGENESIS,
 COCKROACH (1701)
 TRAUMA
 LUNG, CARCINOMA, PATHOGENESIS (1406)*
 NEUROMA, ULTRASTRUCTURE (1402)*
 TUMOR
 ANGIOGENESIS FACTOR, TUMOR VASCULAR-
 IZATION, ISOLATION (1647)
 HEPATOBIILIARY TRACT, MORTALITY,
 SOUTHERN ITALY (1630)*
 ULTRASTRUCTURE
 AMYLOID DEPOSITS, BRONCHIAL ADENOMA,
 OAT-CELL CARCINOMA, MORPHOLOGY
 (1664)
 ANNULATE LAMELLAE, HUMAN NEUROBLASTOMA
 CELLS (1684)
 ANTIBODY-FORMING CELLS, MOUSE SPLEEN,
 FRIEND LEUKEMIA VIRUS (1535)
 BRONCHOGENIC CARCINOMA, SQUAMOUS
 EPITHELIUM (1662)
 CANINE GLIOMA, ROUS SARCOMA VIRUS
 (1484)
 CARCINOMA, THYROID (1714)*
 CILIA, PARATHYROID ADENOMA (1669)
 CLEAR CELL TUMORS, RENAL TUBULES,
 GLYCOGEN METABOLISM, RATS (1352)
 EHRLICH ASCITES, MOUSE CEREBRUM, ACID
 PHOSPHATASE (1684)
 GLIOBLASTOMA HISTOCHEMISTRY, LACTATE
 PRODUCTION (1698)
 LIVER, ETHIONINE NODULES, RAT (1296)
 MALIGNANT CELLS, NUCLEAR POCKETS,
 NUCLEOLUS (1663)
 MEDULLARY CARCINOMA, FLUOROGENIC
 AMINES, THYROID ADENOMA (1654)
 METASTASIS SEQUENCE, WALKER 256 TUMOR
 (1683)
 MORPHOLOGY OF TRANSFORMED CELLS,
 MAREK'S DISEASE VIRUS, HERPESVIRUS
 OF TURKEY (1465)
 MURINE TERATOMAS, EMBRYO IMPLANTATION
 (1671)
 NEOPLASM, INTRACISTERNAL A-PARTICLES,
 VIRUS, MOUSE (1422)
 NEUROMA, TRAUMA (1402)*
 NUCLEAR BODIES, HUMAN TUMORS,
 DIFFERENTIATION CAPACITY (1672)
 RAT TUMOR CELLS, LOW MALIGNANCY, HIGH
 MALIGNANCY (1668)
 RUSSELL'S VIPER, EDEMATOUS MYXOFIBROMA
 C-TYPE PARTICLE, VIRUS (1425)
 SV40, G TYPE POLYPEPTIDE (1497)
 VIRAL PARTICLES, OVINE PULMONARY
 ADENOMAS (1411)
 YABA TUMOR POX VIRUS (1430)
 ETHAN
 NUCLEIC ACIDS, PROTEIN, INTERACTION
 (1362)
 TUMOR INDUCTION, AGE, HAMSTERS (1361)
 PROPORPHYRIN
 EHRLICH ASCITES TUMOR CELLS (1702)

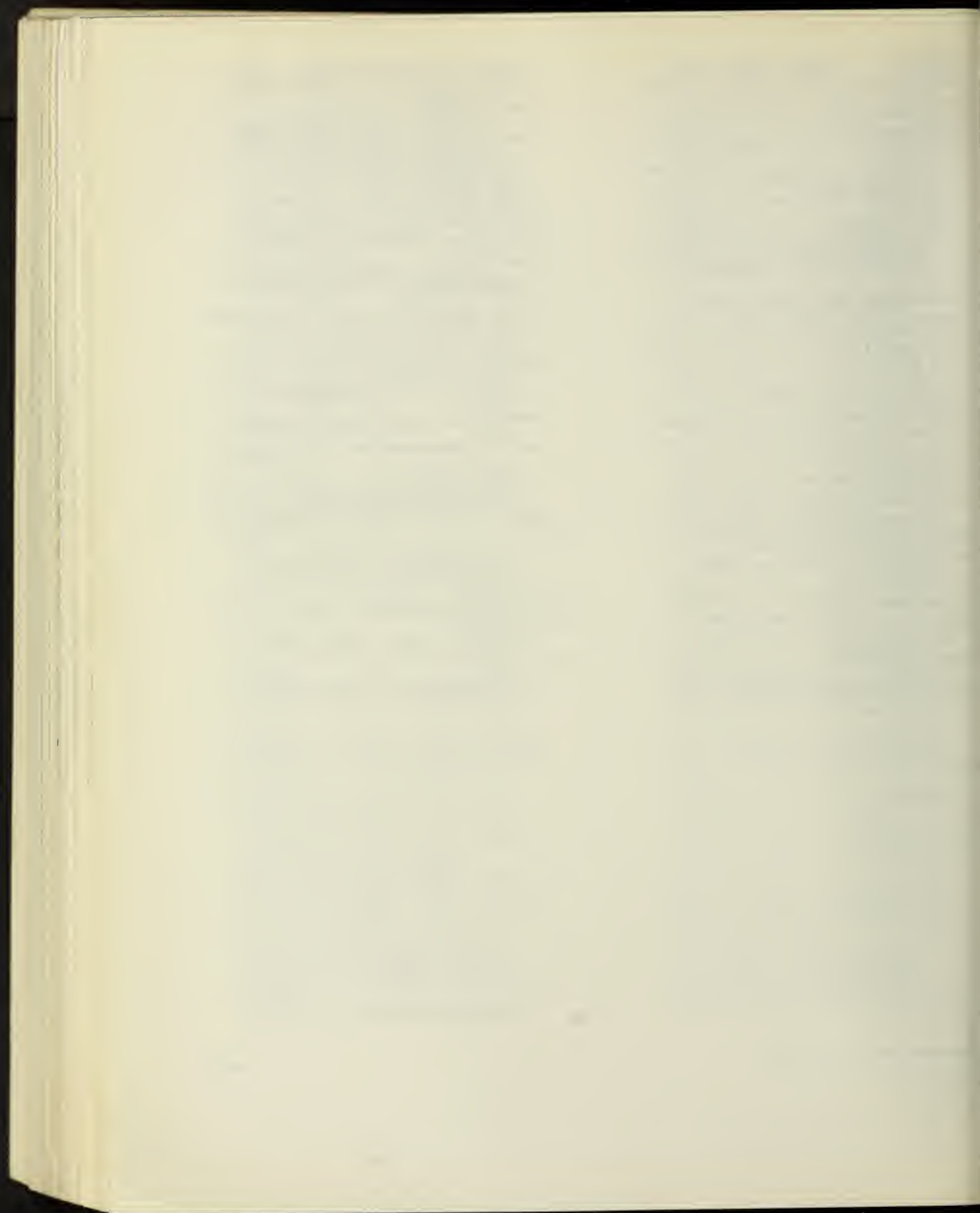
UTERINE CANCER
 OVARIAN CANCER, UNITED STATES
 INCIDENCE (1619)
 UTERUS
 CANCER, CYTOLOGY, SEX CHROMATIN,
 HUMANS (1596)
 CARCINOMA, OBESITY, HYPERTENSION,
 DIABETES MELLITUS (1716)*
 VAGINA
 EPITHELIUM, DIETHYL STILBESTROL,
 CERVIX (1294)
 VIRUS
 ADENOVIRUS 12, DEFECTIVE SIMIAN VIRUS
 40, TUMORIGENICITY (1455)
 ADENOVIRUS 12, T-ANTIGEN, AMINO ACID
 COMPOSITION, HAMSTER (1526)
 ADENOVIRUS 12, TUMOR MORPHOLOGY,
 MOUSE (1456)
 ADENOVIRUS 31, DNA, TEMPERATURE
 MUTANT (1458)
 AVIAN ERYTHROBLASTOSIS, HETEROGENEITY,
 INFECTIVITY (1437)
 AVIAN LEUKOSIS, ROUS SARCOMA, HELPER
 (1439)
 AVIAN SARCOMA, LETHAL MUTANTS TS 75
 AND 149 (1478)
 AVIAN SARCOMA, TRANSFORMED RAT CELLS,
 GENOME (1488)
 BERGOLZ, RETICULOSARCOMATOSIS,
 FREUND'S ADJUVANT, MOUSE (1477)
 C-TYPE PARTICLE, LIVER, FIBROBLASTS
 (1413)
 C-TYPE PARTICLE, PIG KIDNEY CELLS
 (1428)
 C-TYPE PARTICLE, RUSSELL'S VIPER,
 EDEMATOUS MYXOFIBROMA (1425)
 CANCER VIRUS, SV40, NEW CELL LINES,
 KIDNEY (1501)
 CELL-FREE FILTRATE, ANTIGEN, FOCUS
 FORMATION, HUMAN SARCOMAS IN VITRO
 (1427)
 CHICK-EMBRYO-LETHAL-ORPHAN, ANTIGENS,
 CHICK KIDNEY CELLS (1417)
 CHICK-EMBRYO-LETHAL-ORPHAN ADENOVIRUS,
 TUMORS, HISTOPATHOLOGY (1459)
 CHIKUNGUNYA, FIBROBLASTS, LEUKEMIA
 INTERFERON (1628)
 CYTOMEGALOVIRUS, JUVENILE XANTHO-
 GRANULOMA (1518)*
 DEFECTIVE, MOLONEY SARCOMA, MAZURENKO
 LEUKEMIA, MOUSE (1475)
 ENVIRONMENTAL CARCINOGENS, BOTTOM-
 FEEDING FISH, OYSTERS, COMPARATIVE
 ONCOLOGY (1273)
 EPSTEIN BARR, BURKITT'S LYMPHOMA
 (1432)
 EPSTEIN BARR, HODGKIN'S DISEASE,
 ANTIBODY TITERS (1434)
 EPSTEIN BARR, HUMAN LYMPHOBLASTOID
 CELL (1435)
 EPSTEIN BARR, INFECTIOUS MONONUCLEOSIS
 ACUTE LYMPHOCYTIC LEUKEMIA (1578)
 EPSTEIN BARR, LYMPHOBLASTOID CELLS,
 COMPLEMENT-FIXING ANTIGENS,
 BURKITT'S LYMPHOMA (1532)
 EPSTEIN BARR, MAREK'S DISEASE, HERPES,
 ANTIGENIC CROSS-REACTIVITY (1466)

EPSTEIN BARR, MYELOGENOUS LEUKEMIA,
 MULTIPLE NYELOMA, ALL SURFACE (1433)
 FELINE LEUKEMIA, VIRAL RNA (1440)
 FELINE SARCOMA VIRUS, LYMPHOMA,
 TRANSMISSION (1441)
 FRIEND LEUKEMIA, DOUBLE STRANDED
 PENICILLIUM RNA, REGRESSION OF
 SPLENOMEGALY (1450)
 FRIEND LEUKEMIA, IMMUNOSUPPRESSION,
 MOUSE SPLEEN (1529)
 FRIEND LEUKEMIA, INTERFERON, LACTATE
 DEHYDROGENASE (1454)
 FRIEND LEUKEMIA, MACROPHAGE MIGRATION,
 IMMUNITY (1534)
 FRIEND LEUKEMIA, MOUSE SPLEEN,
 ULTRASTRUCTURE OF ANTIBODY-FORMING
 CELLS (1535)
 FRIEND LEUKEMIA, PHAGOCYTOSIS,
 ANTIBODY FORMATION, 7,12-DIMETHYL-
 BENZ(A)ANTHRACENE (1451)
 FRIEND LEUKEMIA, SPLEEN, PARABIOSIS
 (1453)
 FRIEND LEUKEMIA, SURFACE ANTIGENS,
 RAT TUMORS (1533)
 GROSS, LYMPHOMA, CELLULAR AND HUMORAL
 IMMUNE RESPONSE (1531)
 GROSS, MURINE LEUKEMIA, ANTIGEN
 (1523)
 GROSS LEUKEMIA, CYTOTOXIC ANTIBODY
 RESPONSE, LYMPHOMA (1520)
 GROSS LEUKEMIA, IMMUNIZATION OF
 PREGNANT MOTHERS, OFFSPRING IMMUNITY
 (1449)
 HERPES SIMPLEX, INFECTIVITY,
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 (1463)
 HERPES SIMPLEX, LOCALIZATION OF VIRAL
 ANTIGENS, IMMUNOFERRITIN (1521)
 HERPES SIMPLEX, STRUCTURAL PROTEINS
 (1462)
 HERPESLIKE VIRUS, GUINEA PIG,
 ISOLATION AND CHARACTERIZATION
 (1461)
 HERPESVIRUS HOMINIS, SEROLOGICAL
 TYPES, DIFFERENTIAL INFECTIVITY
 (1460)
 HERPESVIRUS SAIMIRI, ACUTE LYMPHOCYTIC
 LEUKEMIA, MALIGNANT LYMPHOMA (1464)
 HERPESVIRUS OF TURKEY, MAREK'S DISEASE
 MORPHOLOGY OF TRANSFORMED CELLS
 (1465)
 HUMAN NASOPHARYNGEAL (1423)
 HYBRID, SV40, ADENOVIRUS 7, TRANS-
 FORMATION (1509)
 INTRACISTERNAL A-PARTICLES, MOUSE
 NEOPLASTIC TISSUE (1422)
 ISOLATE, MAMMARY CARCINOMA, LUNG,
 LEUKOCYTES, MONKEY (1420)
 LEUKOCYTIC LEUKEMIA, HUMAN, EVIDENCE,
 MORPHOLOGY (1418)
 LONG-TERM CELL CULTURE, SUSCEPTI-
 BILITY TO VIRUS, RAT (1412)
 MAMMARY TUMOR, ALLOGRAFT SURVIVAL,
 IMMUNOLOGIC DEFICIENCY (1530)
 MAMMARY TUMOR, AMINOPEPTIDASE ACTIVITY
 (1470)
 MAMMARY TUMOR, COMMON ANTIGENICITY IN

MOUSE TUMORS (1536)
 MAMMARY TUMOR, MOUSE INBRED STRAINS,
 TUMOR INCIDENCE (1471)
 MAREK'S DISEASE, HERPES, IMMUNE
 RESPONSE, CHICKEN (1468)
 MAREK'S DISEASE, HERPESVIRUS, TURKEYS,
 PATHOGENICITY (1467)
 MOLONEY, CELL CULTURES, MITOTIC
 RATES, ANTIGENS (1473)
 MOLONEY LEUKEMIA, C-TYPE PARTICLES
 (1447)
 MOLONEY LEUKEMIA, JLSV-9 CELLS, CELL
 SENSITIVITY (1445)
 MOLONEY LEUKEMIA, STREPTOVIRICIN,
 RNA DEPENDENT DNA POLYMERASE
 INHIBITION (1444)
 MOLONEY LEUKEMIA, TUMORIGENESIS, SOLID
 LYMPHATIC TUMORS, MICE (1443)
 MOLONEY MURINE SARCOMA, RECOVERY FROM
 BOVINE MILK (1474)
 MOUSE MAMMARY TUMOR, ISOLATION,
 HUMAN MILK (1419)
 MURINE LEUKEMIA, DNA, SINGLE- OR
 DOUBLE-STRANDED (1446)
 MURINE LEUKEMIA, INTRACISTERNAL VIRAL
 PARTICLES (1442)
 MURINE LEUKEMIA, LYMPHOCYTIC
 LEUKEMIA, ANTILYMPHOCYTE SERUM
 (1543)
 MURINE LEUKEMIA, MURINE SARCOMA,
 INACTIVATION, ULTRAVIOLET (1452)
 MURINE MAMMARY TUMOR, RNA,
 FLUORESCENCE MICROSCOPY (1469)
 MURINE SARCOMA, GROUP-SPECIFIC ANTIGEN
 (1476)
 MURINE SARCOMA, PATHOLOGY, IMMUNO-
 GENICITY (1472)
 4-NITROQUINOLINE-1-OXIDE, DNA REPAIR
 SYNTHESIS (1356)
 ONCOGENESIS IN MAN, MICROEPIDEMICS
 (1267)
 ONCOGENIC, RNA, DNA, SEQUENCES,
 HYBRIDIZATION (1438)
 PAPILLOMA, WART, KERATIC PAPILLOMA,
 EPIDERMODYSPLASIA VERRUCIFORMIS
 (1516)*
 PARTICLES, OVINE PULMONARY ADENOMAS,
 ULTRASTRUCTURE OF TUMORS (1411)
 POLYOMA, ADENOCARCINOMA, TUMOR ANTIGEN
 (1515)
 POLYOMA, DNA SYNTHESIS, MITOCHONDRIA
 (1513)
 POLYOMA, HAMSTER, INTERFERON INDUCTION
 (1519)
 POLYOMA, HAMSTERS, TRANSFORMED CELLS
 (1421)
 POLYOMA, SUBMAXILLARY GLAND, CHROMO-
 SOME (1512)
 POLYOMA, T ANTIGEN PRODUCTION (1510)
 POLYOMA, VIRUS SYNTHESIS IN VITRO,
 PHLEOMYCIN (1511)
 POLYOMA VIRUS, HAMSTER CELLS,
 GLYCOLIPIDS, PHOSPHOLIPIDS,
 HEMATOSIDES, CERAMIDES (1514)
 PROTEIN SYNTHESIS, NUCLEIC ACID,
 PAPOVA (1426)

* indicates a plain citation without accompanying abstract

RAUSCHER, ANTIBODIES, MOUSE (1448)
 RAUSCHER, 7,12-DIMETHYLBENZ(A)ANTHRA-
 CENE, TRANSFORMATION (1326)
 RNA, RENAL TISSUE, CHICKS, NEPHRO-
 BLASTOMA (1436)
 ROUS SARCOMA, ANTIGEN, CHICK CELLS,
 IMMUNOCHEMICAL CHARACTERIZATION
 (1527)
 ROUS SARCOMA, CHICK EMBRYO, CONTACT
 INHIBITION (1483)
 ROUS SARCOMA, INHIBITION OF FOCUS-
 FORMATION, METHOTREXATE, L-ASPARA-
 GINASE (1480)
 ROUS SARCOMA, PARTICLES, HAMSTERS,
 CHICK CELLS, MAMMALIAN CELLS (1481)
 ROUS SARCOMA, PROTEIN COMPONENTS
 (1482)
 ROUS SARCOMA, TRANSFORMED HAMSTER
 CELLS, VIRAL GENOME (1486)
 ROUS SARCOMA, ULTRASTRUCTURE OF CANINE
 GLIOMAS (1484)
 ROUS SARCOMA, UV ACTIVATION, HELPER
 (1479)
 ROUS SARCOMA, VIRUS-SPECIFIC RNA
 (1487)
 SHOPE PAPILLOMA, EPIDERMAL PAPILLOMAS
 (1522)
 SIMIAN ADENOVIRUS 7, PROPERTIES OF
 VIRUS POPULATION (1457)
 SMALLPOX VACCINATION, FIBROSARCOMA
 (1416)
 SPECIES-SPECIFIC VIRUS, POLIOVIRUS,
 SV40, ADENOVIRUS, POLYOMA (1507)
 SV40, ADENOVIRUS 12, ULTRAVIOLET
 IRRADIATION, BRAIN (1489)
 SV40, ANTIBODY, LABORATORY MONKEY
 HANDLERS (1524)
 SV40, BOVINE, KIDNEY, HAMSTER, LUNG,
 CHROMOSOMES (1491)
 SV40, C-TYPE POLYPEPTIDE (1497)
 SV40, CELL HYBRIDS, UV RADIATION,
 IN VITRO (1517)*
 SV40, CYCLOHEXIMIDE, DNA REPLICATION,
 (1504)
 SV40, DNA FORMS, CYCLOHEXIMIDE (1503)
 SV40, DNA PROPERTIES, KIDNEY (1492)
 SV40, ENZYME ACTIVITY, SIMIAN KIDNEY
 CELLS (1506)
 SV40, FIBROBLASTS, LUNG (1490)
 SV40, HAMSTER CELLS, ANTIGEN (1525)
 SV40, HAMSTER LIVER TISSUE, HAMSTER
 FIBROSARCOMA, ARGINASE (1496)
 SV40, HERPES SIMPLEX, GROWTH IN TRANS-
 FORMED CELLS (1493)
 SV40, INDUCTION OF CELLULAR DNA
 SYNTHESIS (1499)
 SV40, KIDNEY CELLS, ANTIGEN (1538)
 SV40, LUNG, CHROMOSOMES, HAMSTER
 (1498)
 SV40, PROSTATIC CANCER, LACTATE
 DEHYDROGENASE ISOENZYMES, HUMAN,
 HAMSTER (1508)
 SV40, PROSTATIC CARCINOMA, PROGESTOGEN
 TREATMENT (1505)
 SV40, REPLICATION, VIRAL ANTISERUM,
 MONKEY KIDNEY (1495)
 SV40, 3T3 FIBROBLASTS, DENSITY
 INHIBITION OF CELL MOTILITY (1500)
 SV40, UV-IRRADIATED, ANTIGENICITY
 (1537)
 SV40, VIRAL DNA UPTAKE, DEAE DEXTRAN
 (1502)
 VACCINA, TRANSFORMATION, MOUSE EMBRYO
 CELLS (1415)
 VIRUS-LIKE PARTICLES, GASTRIC AND LUNG
 CANCER, LEUKEMIA (1414)
 YABA, THYMIDINE KINASE, TUMORS (1429)
 YABA TUMOR POX, ULTRASTRUCTURE (1430)
 WART
 KERATIC PAPILLOMA, PAPILLOMA VIRUS,
 EPIDERMODYSPLASIA VERRUCIFORMIS
 (1516)*
 WILM'S TUMOR
 HAMARTOMA, CONGENITAL ANIRIDIA (1709)*
 XANTHOGRANULOMA
 JUVENILE, CYTOMEGALOVIRUS, VIRUS
 (1518)*
 YTTERBIUM
 DOSIMETRY, MEDULLARY CANAL, FEMUR,
 RAT (1405)*



U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

OFFICIAL BUSINESS

PENALTY FOR PRIVATE USE, \$300

If you do not desire to continue receiving this publication, please CHECK HERE ☐:
tear off this label and return it to the above address. Your name will then be
promptly removed from the appropriate mailing list.

405
R

*Vet.
Med.*

MARCH-APRIL 1971

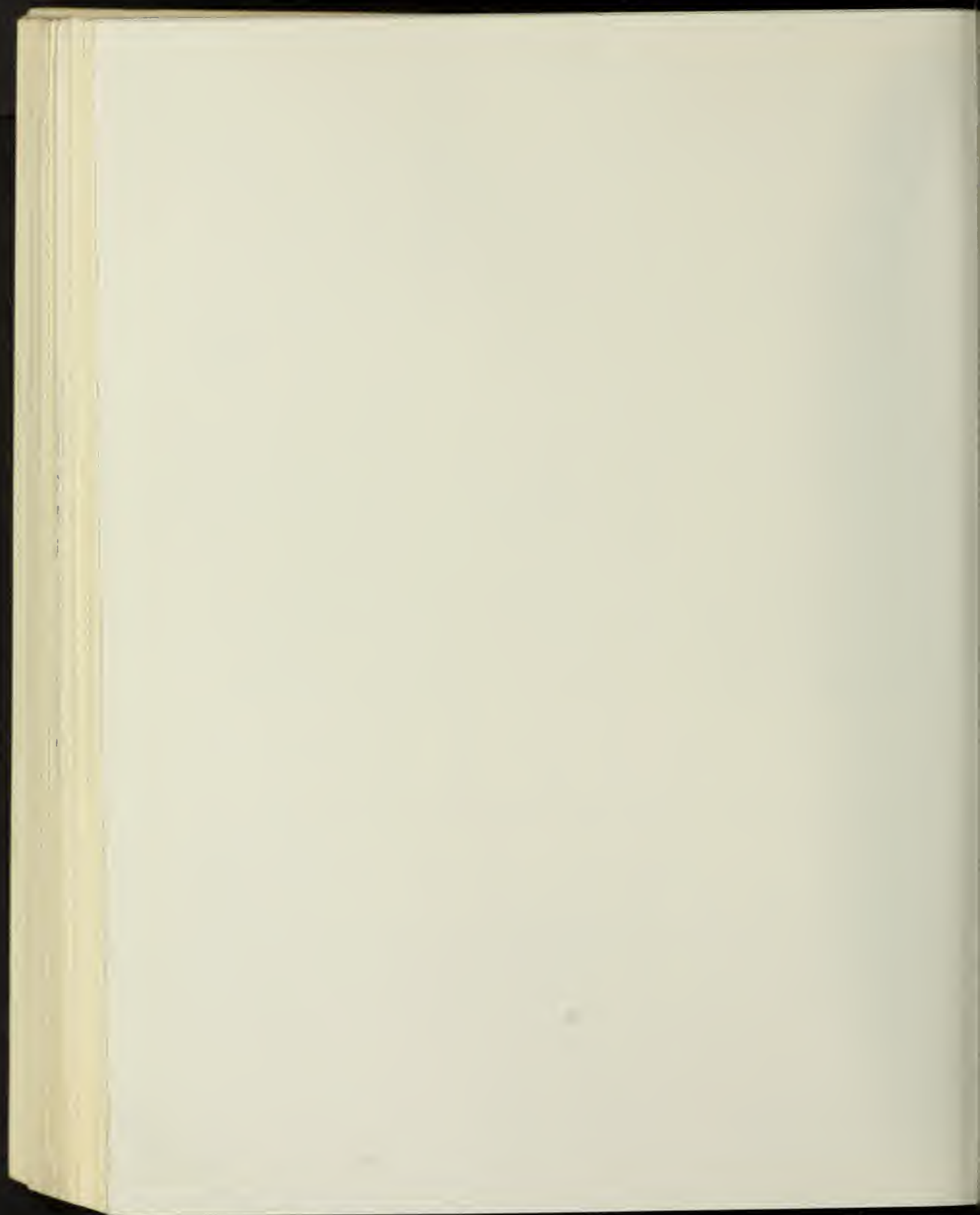
Abstract Nos. 1723-2145



CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health



CARCINOGENESIS ABSTRACTS

A monthly publication of the

National Cancer Institute

Editor

Robert Love, M.D.
Jefferson Medical College, Philadelphia

Associate Editor

George P. Studzinski, M.D.
Jefferson Medical College, Philadelphia

NCI Staff Consultants

Howard R. Rosenberg, M.S.
Sidney Siegel, Ph.D.
Elizabeth Weisburger, Ph.D.

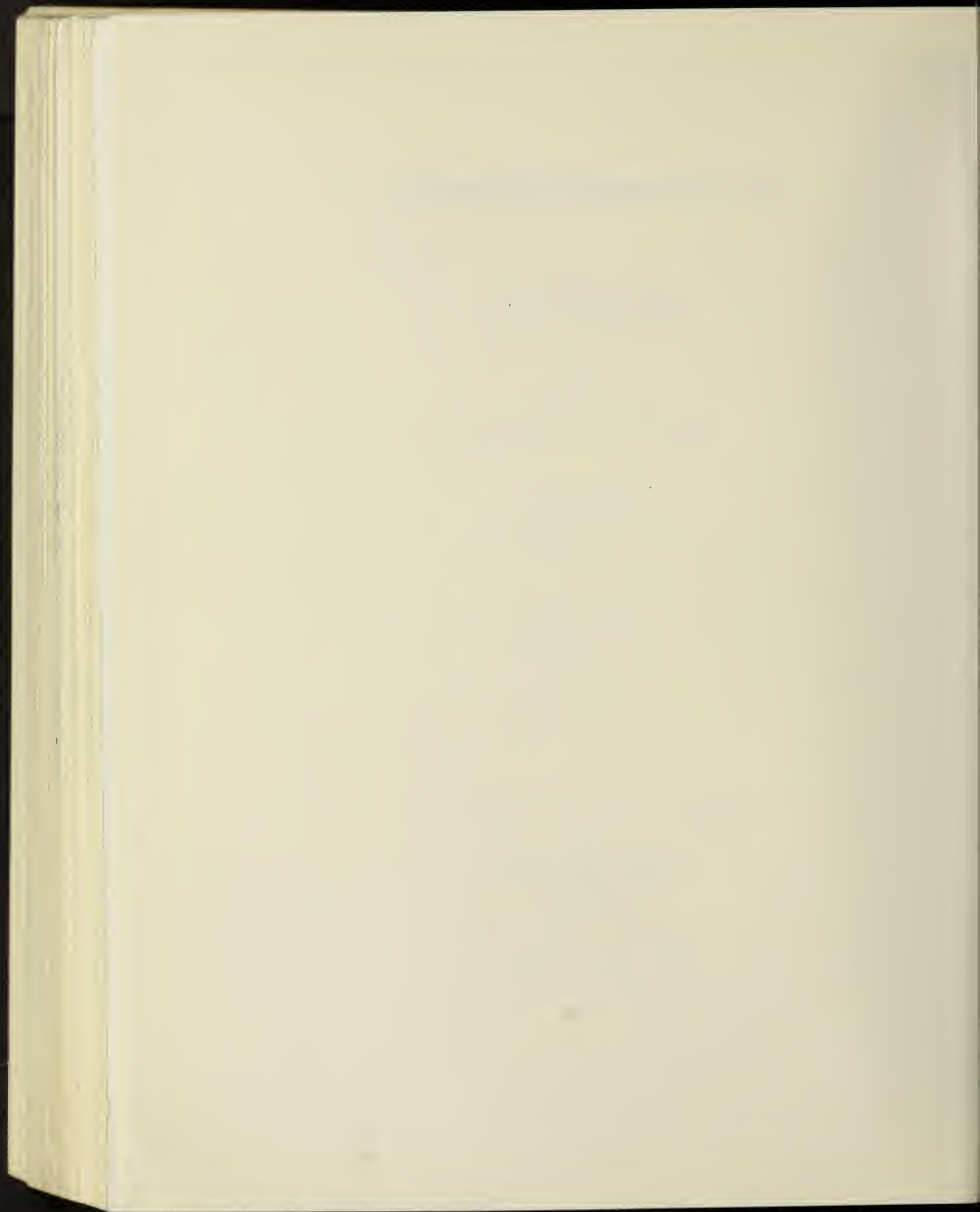
Literature Selected, Abstracted, and Indexed
by

The Franklin Institute Research Laboratories
Science Information Services
Biomedical Section

M. H. Fukami, Ph.D., Technical Editor

Contract Number NIH-71-2073

Public Health Service, USDHEW



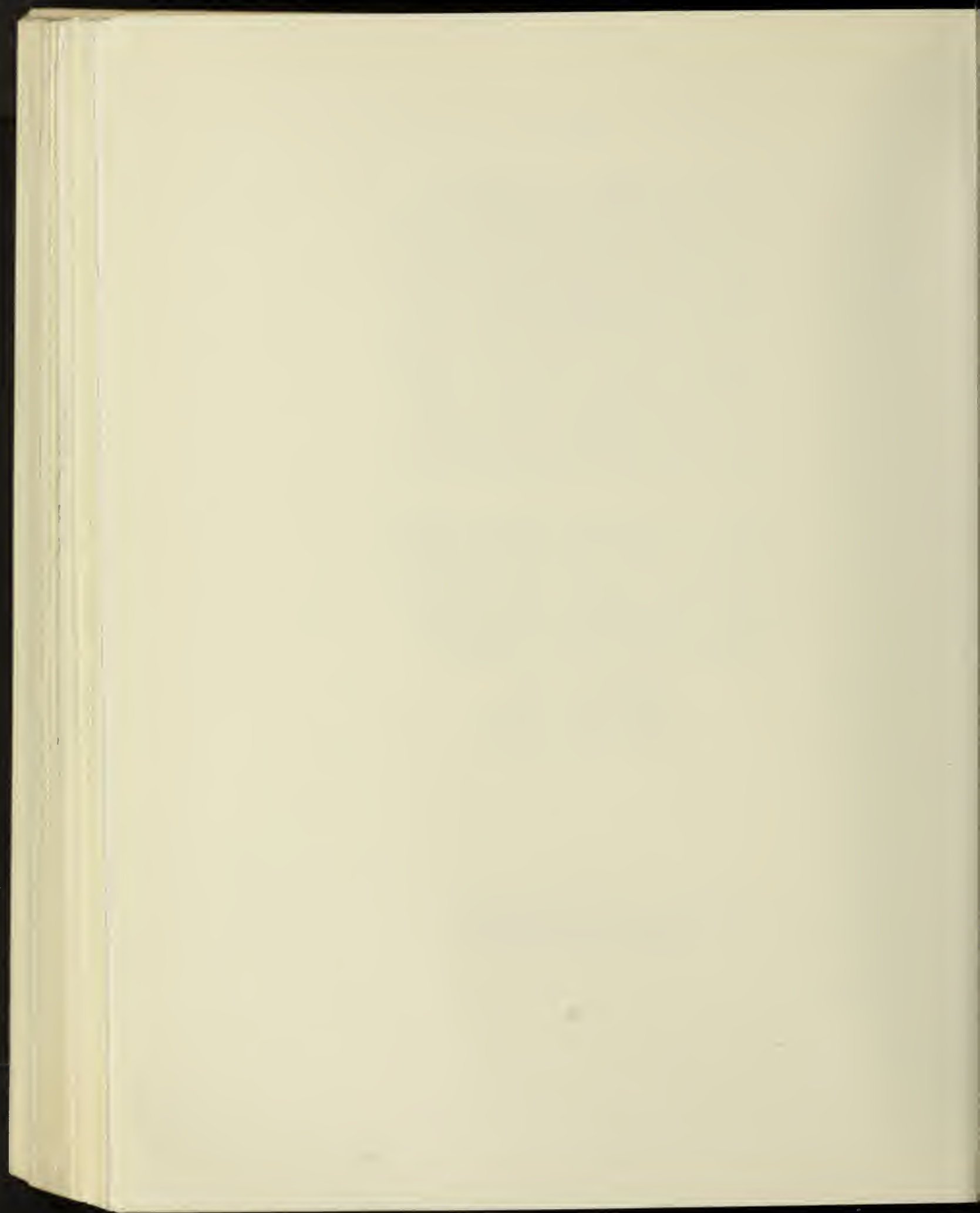
PREFACE

Carcinogenesis Abstracts is a publication of the National Cancer Institute. The journal serves as a vehicle through which current documentation of carcinogenesis research highlights are compiled, condensed, and disseminated on a regular basis. It represents an integral part of the Institute's program of fostering and supporting coordinated research into cancer etiology. Issues of *Carcinogenesis Abstracts* normally contain two-hundred abstracts and twenty citations (unaccompanied by corresponding abstracts). Abstracts and citations refer to the current scientific literature that describes the most significant carcinogenesis research carried on at the National Cancer Institute, other governmental agencies, and private institutions. *Carcinogenesis Abstracts* is intended to be a highly useful current awareness tool for scientists engaged in carcinogenesis research or related areas. The great number and diversity of publications relevant to carcinogenesis make imperative the availability of this service to investigators whose work requires that they keep abreast with current developments in the field.

Carcinogenesis Abstracts is normally published monthly. Volume IX covers the scientific literature published from July 1970 through June 1971. A cumulative subject and author index for Volume IX will be published shortly after the final regular issue. This journal is available free of charge to libraries and to individuals who have a professional interest in carcinogenesis. Requests for *Carcinogenesis Abstracts* from qualified individuals should include statements of their relationship to carcinogenesis research. All correspondence should be addressed as follows:

Carcinogenesis Abstracts
Etiology Area
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20014

Use of Funds for Printing this publication
approved by the Director of the Bureau of
the Budget on July 25, 1967.



NOTE

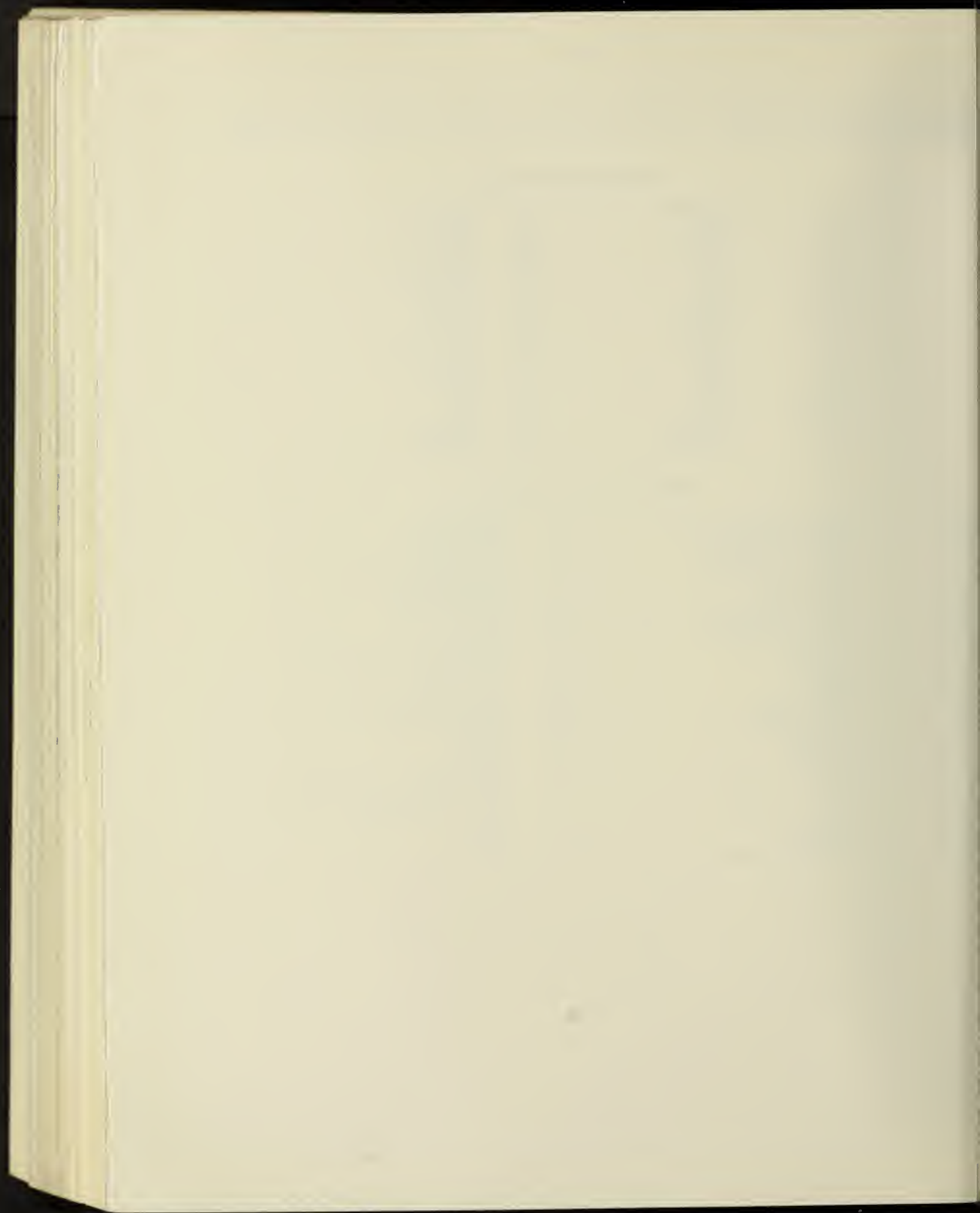
Journal names are abbreviated according to the list of abbreviations used by *Index Medicus*. For journals not covered by *Index Medicus*, the abbreviations (with some modifications) found in *World Medical Periodicals*, 3rd Edition, are used.

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	It.	Italian
Ar.	Arabic	Jap.	Japanese
Bul.	Bulgarian	Kor.	Korean
Ch.	Chinese	Latv.	Latvian
Cz.	Czech	Lith.	Lithuanian
Dan.	Danish	Nor.	Norwegian
Dut.	Dutch	Pol.	Polish
E.	English	Por.	Portuguese
Eston.	Estonian	Rum.	Rumanian
Fin.	Finnish	Rus.	Russian
Fl.	Flemish	Ser.	Serbo-Croatian
Fr.	French	Sl.	Slovak
Ger.	German	Sp.	Spanish
Gr.	Greek	Sw.	Swedish
Heb.	Hebrew	Th.	Thai
Hun.	Hungarian	Turk.	Turkish
Ic.	Icelandic	Uk.	Ukrainian
ln.	Indonesian	Viet.	Vietnamese

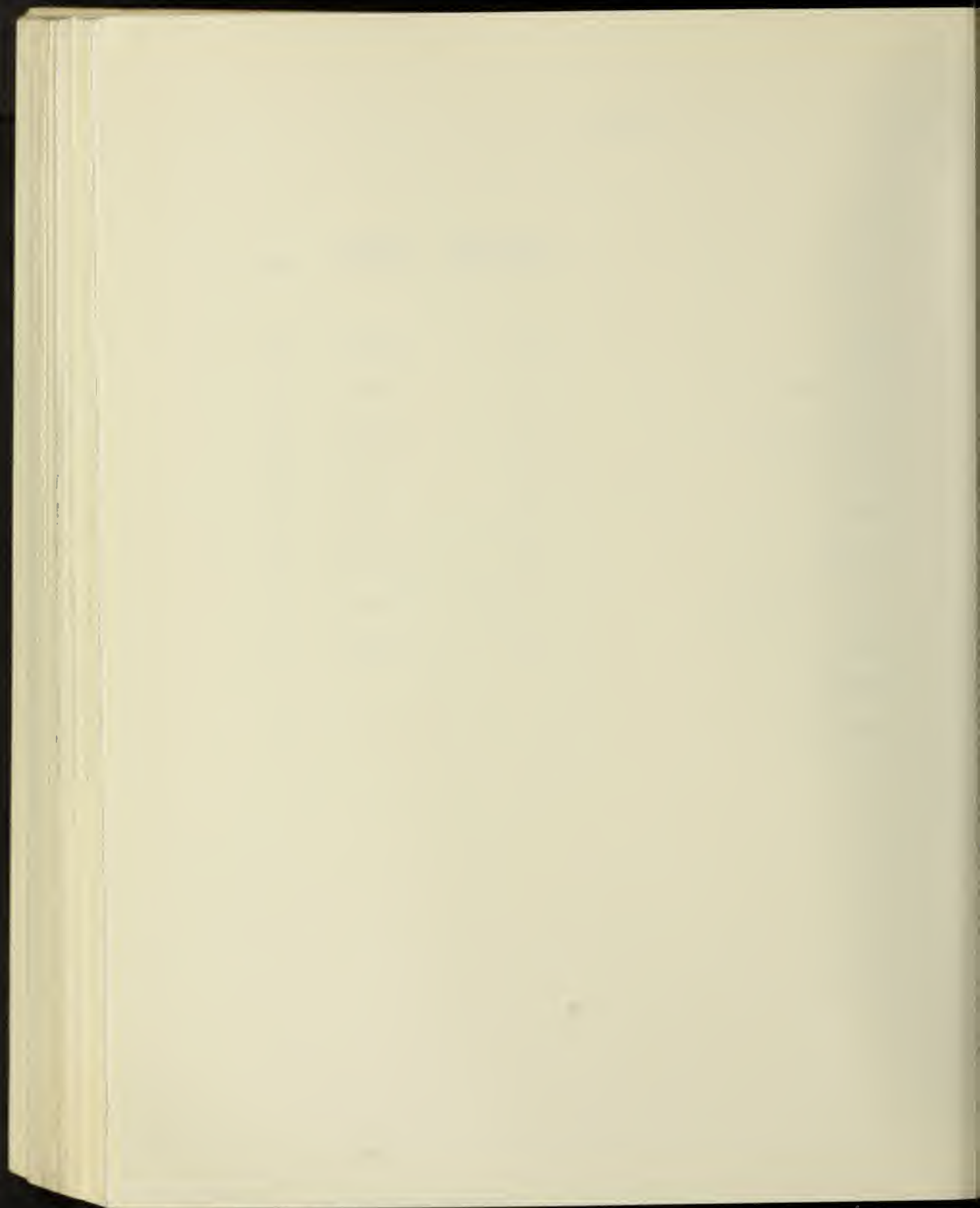
ABBREVIATIONS USED IN ABSTRACTS

adrenocorticotrophic hormone	mg	milligram(s)
adenosine diphosphate	min	minute(s)
adenosine monophosphate	ml	milliliter(s)
adenosine triphosphate	mm	millimeter(s)
degrees centigrade	MTD	maximum tolerated dose
centimeter(s)	ng	nanogram (10^{-9})
central nervous system	pg	picogram (10^{-12})
counts per minute	p.o.	orally
deoxyribonucleic acid	ppm	parts per million
for example	r	Roentgen
gram(s)	RBC	red blood cells (erythrocytes), red blood count
microgram(s)	resp.	respectively
hour(s)	Rev.	review (only in citations)
intramuscular	RNA	ribonucleic acid
intraperitoneal	s.c.	subcutaneous
international unit(s)	sec	second(s)
intravenous	U	unit(s)
kilogram(s)	UV	ultraviolet
median lethal dose(s)	WBC	white blood cells (leukocytes), white blood count
meter(s)	wk	week
molar	wt	weight
milliequivalent(s)	yr	year(s)
millimolar		
micromolar		
milli-,microcurie(s)		



CONTENTS

	Cross Reference Abbreviations	Abstracts, Citations	Page
REVIEW	(Rev)	1723-1760	379
CHEMICAL CARCINOGENESIS	(Chem)	1761-1837	386
PHYSICAL CARCINOGENESIS	(Phys)	1838-1864	403
VIRAL CARCINOGENESIS	(Viral)	1865-1963	409
IMMUNOLOGY	(Immun)	1964-2023	431
PATHOGENESIS	(Path)	2024-2035	444
EPIDEMIOLOGY AND BIOMETRY	(Epid-Biom)	2036-2055	446
MISCELLANEOUS	(Misc)	2056-2145	450
AUTHOR INDEX			i
SUBJECT INDEX			x1



REVIEW

23 DISEASES PREDISPOSING TO LYMPHOID MALIG-
NANCIES. (E.) Drake, B. J. (Northwestern
Med. Sch., Chicago, Ill.), W. A. Caro and S. M.
uefarb. *Cutis* 7(4):413-417, 1971.

herited diseases of immunologic deficiency asso-
ciated with lymphoma development include ataxia-
telangiectasia, Wiskott-Aldrich syndrome and Chediak-
Higashi syndrome. Ataxia-telangiectasia patients
are at an unusually high risk for developing lympho-
sarcoma, reticulum cell sarcoma and Hodgkin's disease,
perhaps reflecting lymphocyte incompetence involved
in this condition as well as humoral and cell-media-
ted immune deficiency. Lymphocyte depletion is also
a feature of the Wiskott-Aldrich syndrome, which pre-
disposes patients to lymphoma. Although humoral and
cellular immune responses in the Chediak-Higashi syn-
drome are normal, patients show an increased suscep-
tibility to lymphoma and viral infection. Among cy-
togenetic disorders predisposing to leukemia are in-
cluded Bloom's syndrome, Fanconi's anemia, Down's
syndrome and Klinefelter's syndrome; in Bloom's syn-
drome an apparent predisposition to malignancy has
been observed but not substantiated in detail. Among
the mastocytoses, urticaria pigmentosa is associated
with an increased risk of leukemia development, most
all leukemia being the predominant form. (16 refer-
ences)

24 CANCER AND DIABETES MELLITUS: A REVIEW
OF THE LITERATURE. (E.) Kessler, I. I.
Harvard Sch. Publ. Hlth., Boston, Mass.) *J Chron*
Dis 23(8):579-600, 1971.

Carbohydrate metabolism tests performed on patients
with cancer of various sites have shown that diabetes
is more common among cancer patients than among non-
cancer patients; the association between pancreatic
cancer and diabetes was found to be especially strik-
ing. Evidence for a similar correlation between can-
cer of the uterine endometrium and diabetes was con-
flicting. Most autopsy-based investigations have in-
dicated that there is a negative correlation between
cancer and diabetes; however, autopsy surveys may be
subject to inherent biases which conceal positive
relations between cancer death and diabetes inci-
dence. Statistical studies of cancer risk among dia-
betic patients have had equivocal results; these stud-
ies have, however, clearly shown that there is a high-
er than normal risk of developing pancreatic cancer
among diabetics. (128 references)

25 SENESCENCE AND JUVENILE FACTORS IN THE
NEOPLASTIC CELL. (It.) Dianzani, M. U.
Inst. General Path. U. Torino, Italy). *Giorn*
Patol 18(4):245-279, 1970.

In a review of the literature of the relationship
between aging and carcinogenesis, note was taken
of the fact that experimentally induced tumors oc-
cur mostly in young animals, while spontaneous
tumors occur mostly in animals of advanced age.
Normal cells and cancer cells are not similar bio-
chemically or morphologically; however aging and

the process of carcinogenesis may act upon elements
common to aged cells and cancer cells. The theory
that aging is a result of lifelong exposure to
irradiation may provide insight into the relation-
ship between aging and carcinogenesis, for it is
known that cancer can result from exposure to ir-
radiation. (185 references)

1726 MICROORGANISMS ASSOCIATED WITH MALIGNANCY.
(E.) Pease, P. (Dept. Bacteriol., U. Birmingham,
England). *Ann NY Acad Sci* 174(2):782-785, 1970.

A group of related bacteria have been found in
association with malignancies in the newt and
may be associated with human tumors. These bacteria
are gram-positive, weakly acid-fast, and vary in
morphology from small spheres to long rods. There
is evidence which suggests the possibility that
bacteria of this type in the L-form resemble the
Rous sarcoma virus and may even be identical with
this carcinogenic virus. Bacteria of the group
in question are widespread in nonmalignant
patients as well as in patients with cancer; it is
suggested that, if the microbes have a causal connec-
tion with cancer, their efficacy may depend on unus-
ually large quantities of bacteria accumulating in
a single patient. There is reason to believe that
the group of bacteria discussed are members of the
Mycococcus bacteria class. Other bacteria found in
association with malignancy are *Agrobacter* and
Listeria group organisms. (29 references)

1727 PARASITISM AND CANCER. (Fr.) Juminer, B.
(Inst. Pasteur, Tunis). *Arch Inst Pasteur*
Tunis 47(3):211-227, 1970.

A review of the medical literature does not support
either the etiological or pathogenic relationship
of cancer to parasitism. Although cestodes in ani-
mals and trematodes in humans have been found in
some organs together with cancer, and although bil-
harziasis and cancer of the bladder have been
found simultaneously, the arguments against there
being a causal relationship are strong. There is
some indication that toxoplasmosis may be linked
to primary cancer of the nervous system, but the
evidence for this is still meager. The connection
between the pathogenesis of cancer and the parasitic
etiology is founded on a predisposition for the ter-
rain to favor the development of both diseases, a
specific role of certain metabolites either produced
or induced by the parasite, or a true carcinogenic
power organically related to the parasite. However,
these connections are derived for the most part from
epidemiological data and no valid experimental evi-
dence exists that this relationship is causal. (47
references)

1728 CELLULAR COMMUNICATION, CONTACT INHIBITION,
CELL CLOCKS AND CANCER: THE IMPACT OF THE
WORK AND IDEAS OF W. R. LOEWENSTEIN. (E.) Burton,
A. C. (Dept. Biophys., U. Western Ontario, London,
Canada). *Perspective Biol Med* 14(2):301-318, 1971.

Theories of cellular interaction for normal and malignant cell proliferation are discussed. Loewenstein's discovery that normal liver cells exchange substances of high molecular weight while cancer cells have little intercommunication prompted the hypothesis that all living cells retain the ability to divide, and that living cells divide or remain in interphase as a result of intercellular factors. Such intercellular factors, which promote cellular intercommunication, may be mediated by the electrical resistance between neighboring and distant cells. This suggests that malignant cells differ from normal cells in that the former do not freely communicate with other cells in contact with them. The breakdown in intercellular communication, according to this theory, triggers malignant proliferation. In normal cell systems, contact inhibition operates by providing individual cells with "information" as to the optimal size of the cell colony, restraining the cell from division. For contact inhibition to operate, one substance within the cell must have a concentration gradient which regulates cell division and which is altered by neighboring cells. Agents which reduce communication between cells or which cause cells to divide synchronously would reduce contact inhibition or preclude it altogether, leading to malignant cell proliferation. Radiation in this theory might be considered carcinogenic because cells recovering from radiation damage become synchronous. An upset in the regular rhythm or cycle of biochemical events in cells might also promote malignant proliferation, even in instances when cells are not synchronous and intercellular communication is satisfactory. (22 references)

- 1729 A NEW CONCEPTUAL FRAMEWORK FOR SARCOMA.
(E.) Siegler, R. (Boston U. Med. Sch.,
Mass.) *Bibl Haemat* 36:257-260, 1970.

Spontaneous reticulum cell sarcomas of mice and Moloney virus-induced mouse sarcomas were studied in an attempt to arrive at a comprehensive theory of pathogenesis for sarcomas as opposed to carcinomas. While carcinomas appear to grow by clonal proliferation of a population of malignant cells originating from a single mutant cell, sarcomas do not grow by clonal proliferation of daughter cells. Both sarcoma systems studied appeared to grow by the continuous recruitment by the tumor cells of adjoining normal tissue. Animals dying of sarcomas may die because they are unable to check the spread of malignant tumors to normal tissue, and not because they are preyed upon by a genetically-determined population of malignant cells as in carcinoma. Whether a sarcoma induced by virus ultimately kills the affected animal appears to depend on whether or not the spread of the sarcoma has impinged upon vital organs; hence, the presence of an effective immune response to impede or halt the spread of the sarcomas in affected animals was crucial for their survival. Proliferative lesions of the mesenchyme are probably a normal physiologic response designed to repair tissue injury; when host immune mechanisms are inadequate to check the repair proliferation of cells, the lesion produced by this proliferation will be of the type called "sarcoma". (2 references)

- 1730 THE PHILADELPHIA CHROMOSOME. (Ger.)
Hossfeld, D. K. (Roswell Park Mem. Inst.,
Buffalo, N. Y.) and A. A. Sandberg. *Klin Wschr*
48(24):1431-1441, 1970.

The presence or absence of the Philadelphia chromosome (Ph¹) in karyotypes of patients with chronic myelocytic leukemia (CML) divides these patients into those with good prognoses and those with poor prognoses, resp. Ph¹ positive males with CML who lack a Y chromosome in leukemic cells have especially favorable prognoses. Although it is most regularly associated with CML, the Ph¹ chromosome has also been found in patients with acute myeloblastic leukemia, polycythemia, myeloid metaplasia and thrombocytopenia. Although chromosomal aberrations other than Ph¹ chromosome occur in more than 65% of CML patients, it has not been shown that these anomalies cause the blastic transformation associated with CML. Ph¹ chromosome-like deletions have been produced by exposure to ionizing radiation. There is some reason to believe that the Ph¹ chromosome may originate in a differentiated cell type, rather than in an altered stem cell. (174 references)

- 1731 ULTRASTRUCTURAL ALTERATION OF THE MITOCHONDRIAL ELECTRON TRANSPORT CHAIN INVOLVING ELECTRON LEAK: POSSIBLE BASIS OF "RESPIRATORY IMPAIRMENT" IN CERTAIN TUMORS. (E.) Arcos, J. C. (U.S. Publ. Hlth. Serv. Hosp., New Orleans, La.). *J Theor Biol* 30(3):533-543, 1971.

The decrease in the high amplitude swelling and contraction of tumor mitochondria is hypothesized to be due to an absent or severely altered mechanochemical effector system. Alterations in this system which is normally linked to the electron transport chain are also considered to be associated with the changes in fatty acid, phospholipid and cholesterol metabolism known to occur in tumor tissues. The altered cellular lipid pattern may result in lesions of tumor mitochondria such that leakage of electrons from the chain may occur. Substrate oxidation may then proceed as normally, but a fraction of the electrons may not reach the terminal acceptor, oxygen, resulting in a decrease of the respiratory rate. (69 references)

- 1732 KINETICS OF THE PROLIFERATION OF CANCER CELLS. (Fr.) Stryckmans, P. (Jules Bordet Inst. Tumor Ctr., Free U. Brussels, Belgium). *Acta Chir Belg* (Suppl. 1):7-17, 1971.

The growth of a tumor represents the breakdown of the state of equilibrium of normal tissues, and involves inequality of cell production and cell loss. The growth of tumors has been measured by its volume doubling time, implying an exponential growth. This concept was disputed by Laird who studied the normal growth of a guinea-pig from 40 days before its birth to 140 days after and described this growth by an asymmetrical sigmoid curve (Gompertz equation), showing an exponential diminution in the rate of growth. Tumors from 3 species of animals

(rat, mouse, rabbit) were shown to develop along this type of curve. The cellular loss may be due to different factors (cellular death; maturation in different compartment, desquamation or emigration) and should be determined. Observations made on the growth of metastases of human tumors are only valid for that metastasis; others in the same patient may have a different rate of growth. This indicates that the total population of tumor cells in the organism may be extremely heterogeneous and that the parameters of production may vary from one location to another, as would the chemotherapeutic effect. (21 references)

733 REFLECTIONS ON LATENT VIRUSES - A NEW DEFINITION OF AN INFECTIOUS AGENT. (E.) Hirschman, S. Z. (Mount Sinai Sch. Med., City U. New York, N. Y.). *Mt Sinai J Med* 38(2):257-266, 1971.

Recent experimental work on latent virus infection has been reviewed, and hypotheses accounting for the activation of a latent virus infection and subsequent malignant progression were aired. It has been shown that various RNA viruses, including murine leukemia and sarcoma viruses, may be present in a latent state in animal tissues, and that virus replication may be triggered by serial passage of the host cells or by irradiation. The discovery of an RNA-dependent DNA polymerase suggests a mechanism for the beginning of overt infection and viral replication of latent viruses. Viral RNA may synthesize DNA in the host cells; more viral DNA may then be produced by means of a DNA-dependent DNA polymerase, and the new DNA would code for the production of viral RNA, initiating viral replication. Such a hypothesis would account for the stimulation of DNA synthesis by RNA viruses, the spontaneous appearance of RNA leukemia virus in mouse cells, and the induction of leukemia by X-irradiation. Models for viral replication which would account for the viral latent state were also discussed. A virus may consist in some cases of protein which can induce normally inactive or "switched off" host cell DNA to reproduce the same proteins (the "self-induction" theory). Possible candidates for such a proteinaceous virus might be the Australia antigen and certain so-called "slow-growing" viruses. (38 references)

734 THE VIRAL THEORY OF CANCER AND EXPERIMENTAL ANTICANCER IMMUNITY. (Fr.) Gross, L. (VA Hosp, Bronx, N. Y.). *Bull Inst Pasteur* 69(2):193-208, 1971.

Experiments supporting the viral theory of cancer are reviewed, including among others: viral induction of leukemia and lymphosarcoma in mice; erythroblastosis and myeloblastosis in birds; visceral lymphomatosis in chicks (transmissible via the egg or by the airborne route); lymphosarcoma and fibrosarcoma in cats. The viral characteristics have been verified in most cases by electron microscopy. Potential oncogenicity of latent viral material has been demonstrated in anti-blepharitis vaccines from monkey kidney cell cultures which contain traces of SV40 virus contaminant capable of inducing sarcoma in newborn hamsters.

Latent human adenovirus has been shown to produce sarcoma in rats, mice and newborn hamsters. Although proof is lacking for viral transmission of cancer in man, it is reasonable, from evidence in animals, to formulate an hypothesis whereby the activation by external (chemical compounds, radioactivity, etc.) or internal (hormones, abnormal metabolites, etc.) stimuli of latent oncogenic viruses in one organism produces active oncogenesis. Immunization against experimentally induced cancer in animals by injection of minute amounts of neoplastic cells has been demonstrated. (53 references)

1735 STRAIN MC29, AN AVIAN LEUKOSIS VIRUS OF UNIQUE PROPERTIES. (E.) Langlois, A. J. (Duke U. Med. Ctr., Durham, N. C.), D. Beard and J. W. Beard. *Bibl Haemat* 36:96-105, 1970.

An avian leukosis virus, strain MC29, having properties distinguishing it from other leukosis viruses, is described. MC29 causes principally myeloid and renal tumors; mesothelial growths and hepatocytomas have also been associated with MC29 virus. Chick embryo cells in culture respond rapidly to infection with MC29, as measured by release of virus. Cells transformed by MC29 *in vitro* alter in morphology soon after infection. MC29 is antigenically similar to other leukosis viruses including Rous sarcoma virus and strain BAI. (50 references)

1736 MYELOMA PROTEINS (M-COMPONENTS) WITH ANTIBODY-LIKE ACTIVITY. (E.) Potter, M. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *New Eng J Med* 284(15):831-838, 1971.

Five antigens for which multiple "M-components" have been found were discussed; M-components were defined as antigen-binding homogeneous immunoglobulins produced by benign or malignant monoclonal disorders. Among M-components with antibody-like activity, the anti-IgG or rheumatoid factors have been found in 2-20% of normal persons and in 75-100% of patients with rheumatoid arthritis. The highest titers of rheumatoid factors have been found in patients with malignant monoclonal disorders. The chemical nature of the rheumatoid factor has yet to be precisely described. Antistreptolysin O has been found in the sera of patients with multiple myeloma and in patients with benign monoclonal disorder. Cold agglutinins, including anti-I and the I antigen system, may arise in the body from an exogenous source. M-components having anti-lipoprotein have been described in patients with multiple myeloma, hyperlipidemia and xanthomatosis. Plasma cell tumors induced in mice produced antipolysaccharide and antiphosphoryl choline IgA myeloma proteins. The antigens eliciting the M-component reaction include bacteria in the gastrointestinal tract. M-components which bind antigen may arise from the stimulation to malignant growth by antigens of a clone of cells, or as a result of an abnormal adjuvant effect stimulating the immune system. (53 references)

- 1737 IMMUNOCYTOMA O' MICE AN' MEN. (E.) Hobbs, J. R. (Westminster Med. Sch., London, England). *Brit Med J* 2(5753):67-72, 1971.

The growth of a monoclonal of cells (an immunocytoma) is indicated when narrow bands which can be identified as being due to a single type of immunoglobulin are formed on electrophoresis; the growth of such cells is monitored by measuring paraprotein levels and looking for evidence of dedifferentiation. For an ascitic form of plasmacytoma, estimates of the actual total number of plasmacytoma cells in a mouse were obtained by isotope dilution and a positive correlation with the serum level of paraprotein was demonstrated. It was further shown that such tumor growth was exponential in mice. For human patients screened for the M.R.C. Myeloma Trials, the rise of serum IgG or IgA paraprotein levels, or the 24-hr urinary output of Bence Jones protein was also found to be exponential. Studies of plasmacytoma in mice and men indicate that it takes some 21 yr from the time a single plasma cell precursor is transformed for clinical IgA myelomatosis to become apparent. Bence Jones proteins were found to be free monoclonal light chains resulting from an imbalance in heavy and light chain synthesis by malignant myeloma cells, presumably through dedifferentiation. Four features useful in predicting a benign or malignant immunocytoma were presented. The use of high dosages (1 mg/kg body wt) of drugs such as melphalan and cyclophosphamide for short periods was recommended in treating myelomatosis. (35 references)

- 1738 REVIEW OF THE PRESENT STATUS OF RESEARCH IN TUMOR SPECIFIC TRANSPLANTATION ANTIGENS IN HUMAN LEUKEMIA. (Ger.) Zintl, F. (U. Child Clin., Jussuf Ibrahim, Jena, Germany) and W. Plenert. *Folia Haemat* 95(1):1-20, 1971.

A review of tumor induction in mice by means of viral carcinogens is presented, and some findings in man of virus-like particles in lymph nodes, bone marrow and blood plasma concentrates from acute lymphatic leukemias and chronic myeloses are reported. Mixed virus-like particles have also been found in infectious mononucleosis. Immunological studies relating lymphatic, myeloid, reticular and erythroblastic leukemias are described. Human leukemia and lymphomas in connection with tumor specific transplantation antigens (TSTA) are reviewed, including the isoantigens of leukemia cells, Burkitt's lymphoma, Epstein-Barr virus, cellular defense mechanisms against TSTA of human leukemia (by *in vivo* and *in vitro* experiments) as well as humoral defense mechanisms, and heterologous, homologous and autologous antisera against leukemic cells. Therapy is discussed with special attention to immunostimulation in contrast to immunosuppression. (124 references)

- 1739 IMMUNOLOGICAL STUDIES ON BURKITT'S LYMPHOMA. (E.) Klein, G. (Karolinska Inst., Stockholm, Sweden). *Postgrad Med J* 47(545):141-155, 1971.

Recent developments concerning the antigenic properties of Burkitt's lymphoma are reviewed and discussed. When fresh Burkitt's lymphoma biopsy cells were exposed to sera from patients with Burkitt's lymphoma and other malignancies and to sera from patients with nonneoplastic disease, indirect membrane immunofluorescence tests indicated that the Burkitt's lymphoma sera contained an attached immunoglobulin which was not found in sera from other patients. The degree of immunoglobulin coating on the surface of the biopsy cells was found to vary. The immunoglobulin appeared to be IgM and/or IgG. The membrane antigen found on Burkitt's lymphoma cells was thought to be determined by the genome of the Epstein-Barr virus which is found in some Burkitt's lymphoma cells in culture. Recent evidence has suggested that the antigen may represent a viral envelope component. Serological studies of various populations relative to Burkitt's lymphoma have indicated that serological anti-Epstein-Barr virus activity is widespread in all human communities. The disease-related distribution of anti-virus antibody patterns is discussed, and it was noted that there is preliminary evidence that the antibodies against the soluble Epstein-Barr virus antigens appear during tumor growth and decline in number during tumor regression. It was not certain whether the virus-associated membrane antigens are essential for the neoplastic development of cells in Burkitt's lymphoma. (111 references)

- 1740 INTERACTION OF HOST AND CANCER: THE POTENTIAL ANTIGENICITY OF CANCER CELLS, THE DEFENSE MECHANISMS OF CANCER PATIENTS, AND THE INFLUENCE OF ENDOCRINE GLANDS AND AGING ON CANCER. (E.) Mulligan, R. M. (U. Colorado Sch. Med., Denver). *Exp Med Surg* 28(1):1-17, 1970.

Electron microscopic studies reveal a proportionate host response to the complexity of structures within cancerous cells indicative of protein elaboration, delayed hypersensitivity and antibody production in patients with non-hematopoietic cancer. Patients with lymphopoietic cancer display decreased resistance to infection and interference with synthesis of globulins of 7S and 19S types. Increased nucleic acid synthesis, heightened activity of melanoblasts, decreased differentiation of epithelial and lymphopoietic cells relative to the alteration in somatotrophin, melanotrophin and thyroglobulin production, delayed or declining immune competence of thymus and lymphoid tissue in childhood and adult life, resp., antimetabolic effects of hydrocortisone, and decreased secretion of sex hormones all favor the induction of carcinoma. (40 references)

- 1741 THE HEALTH MENACE OF TOBACCO. Ochsner, A. (Ochsner Clin., New Orleans, La). *Amer Sci* 59(2):246-252, 1971.

The epidemiological evidence establishing a causal connection between tobacco use and cancer is rehearsed. The increase in mortality from lung cancer in the United States between 1930 (2,500 deaths) and 1964

43,100 deaths) appears to be related to the fact that cigarette smoking did not become a widespread practice in the United States until the time of the First World War. Statistics from Iceland show that lung cancer mortality began to increase in that country around 1955, and that cigarette smoking became prevalent in Iceland during the Second World War. Adenocarcinoma of the lungs does not appear to be associated with smoking. It also appears that the chance of developing cancer decreases among those who stop smoking, the decrease accompanying the time elapsing since cessation of smoking. Other cancers caused by smoking include laryngeal cancer, which is also on the rise in the United States, lip, tongue and oral cancer, esophageal cancer and cancer of the urinary bladder. Bladder cancer is thought to be caused by cigarette smoke interfering with metabolism in such a way as to promote the excretion of carcinogens in the urine. (50 references)

1742 CONTRACEPTION AND CANCEROGENIC RISKS. (Fr.) Cappelaere, P. (no affil). *Lille Med 16 Special*:45-51, 1971.

From experimental findings in animals and from cytological evidence, the use of intrauterine devices for contraception have led to either an inflammatory process close to the uterus which can disappear after removal of the device, the development of an epidermoid metaplasia followed by a squamous epithelioma, or to a persistent chronic inflammatory lesion which favored the development of an endometrial adenocarcinoma. However, none of these manifestations were found in humans including the intermediary stage of epidermoid metaplasia. The use of hormonal contraception, as well as hormone therapy, is not considered as favoring the development of cervico-uterine cancer, and neither uterine (or endometrial) nor mammary cancers have found clinical confirmation attributable to hormonal contraceptives. (65 references)

1743 STEROID CONTRACEPTIVES. (E.) Vande Wiele, R. L. (Coll. Phys. Surg., Columbia U., New York, N. Y.). *Gynec Invest 1*(suppl.):55-66, 1970.

The chemistry and physiological modes of action of steroid contraceptives were described in a brief descriptive review, and the changes in certain body systems induced by these agents were considered. Functions which are influenced to one degree or another by ingestion of oral contraceptives include ovarian function, carbohydrate and lipid metabolism, protein metabolism, liver function and circulation. Statistics were produced indicating that users of steroid contraceptives are at a higher risk than nonusers of developing thromboembolic diseases. Despite recent studies which suggest that women taking oral contraceptives have an increased prevalence of abnormal Papanicolaou smears and possibly of carcinoma *in situ* of the cervix, there was thought to be no reason to believe that use of steroid contraceptives affects the incidence of cancer either positively or negatively. (6 references)

1744 AFLATOXINS. (E.) Wogan, G. N. (Dept. Nutr. Food Sci., Massachusetts Inst. Tech., Cambridge) and R. S. Pong. *Ann NY Acad Sci 174*(2): 623-635, 1970.

The biogenesis, chemical nature, and the biological and chemical effects of aflatoxins is summarized. Aflatoxin-producing fungi are widely dispersed in air and soil, are capable of growth on a wide variety of natural substrates, chiefly grains, exhibit a strong fluorescence in ultraviolet light, and can readily be separated by thin-layer chromatography in various fractions. Their relative solubility in polar organic solvents and sparing solubility in water has been utilized in the development of physicochemical assays for their detection and quantitation in foods. *In vivo* studies have revealed a relationship between chemical structure and acute lethality with B₁ being most toxic, followed by G₁, B₂, and G₂ in decreasing potency; *in vitro* studies have shown the aflatoxins to be capable of inducing mitotic inhibition as well as chromosome aberrations. The carcinogenic capacity of aflatoxin has been demonstrated in rats, ducks, trout and ferrets, and has been shown to be enhanced by protein depletion and liver cirrhosis in the rat, in which it is inhibited by hypophysectomy. Aflatoxin inhibition of DNA synthesis has been seen subsequent to partial hepatectomy, and changes in hepatocyte nuclear fine structures have revealed that the agent affects RNA metabolism in rat liver. Their hepatotoxic and carcinogenic properties in animals give particular importance to questions concerning their possible public health significance. (80 references)

1745 BIOPHYSICS (4-NITROQUINOLINE-1-OXIDE). (E.) Nagata, C. *Rec Results Cancer Res 34*:17-31, 1971.

Based upon the electronic structural features of 4-nitroquinoline-1-oxide, it was predicted that a charge transfer complex would form between this molecule and the DNA base adenine. The quantity of charge transferred to 4-nitroquinoline-1-oxide (4-NQO) and its related compounds correlated well with their carcinogenicity. Physical binding of 4-NQO to DNA was proved *in vitro*. The orientation within DNA was parallel to the base planes, and the affinity for purine bases was stronger than that for pyrimidine ones. Maximum binding occurred at ratios of DNA to 4-NQO greater than 7 to 1. *In vitro* experiments indicated that 4-NQO and 4-hydroxyaminoquinoline-1-oxide (4-HAQ) bind covalently to the bases of nucleic acids, whereas no such binding was shown for non-carcinogenic quinoline-1-oxides. The amount of 4-NQO bound is about 1 molecule/10⁴ nucleotides of DNA, whereas for 4-HAQ there is approximately 0.5-1.5 molecule/1000 nucleotides of DNA. Binding to SH compounds such as cysteine and glutathione was demonstrated for 4-NQO and a charge transfer complex with protein or aromatic amino acids was also shown. UV irradiation of 4-NQO in the solid state or in organic solvents resulted in free radical formation. ESR signals in dioxane, hexane and benzene differed from each other, indicating that different kinds of

free radicals were formed according to the solvents used. In hexane and benzene the unpaired electron is localized on the nitro-group nitrogen atom whereas in dioxane it is delocalized. Without photoirradiation, 4-HAQ was found to convert oxidatively to a free radical, the structure of which was determined with the aid of ^{15}N and/or D replacement method. Free radical formation is considered to have some influence on the oxidation-reduction processes of biological systems and play an important role in the carcinogenic processes of these compounds. The photodynamic activity of 4-NQO on *Paramecium caudatum* was found and a relationship was observed between photodynamic activities and carcinogenicities of quinoline-1-oxides. This relationship does not hold for 4-HAQ and its derivatives. Photoirradiation of 4-NQO in the presence of nucleic acids, resulted in the destruction of the guanine moiety. (References)

- 1746 CARCINOGENICITY (OF 4-NITROQUINOLINE-1-OXIDE). (E.) Endo, H. (no affil). *Rec Results Cancer Res* 34:32-52, 1971.

Experimental carcinogenesis induced by 4-nitroquinoline-1-oxide in varying doses and methods of administration and in varying animal systems was reviewed. More than 65 experiments in which 4-nitroquinoline-1-oxide or one of its derivatives were given to rodents (including mice, rats, hamsters and guinea pigs) were tabulated. Topical painting of the carcinogen appeared in general to produce a higher incidence of tumors in recipients than did injection. Common types of tumors induced by 4-nitroquinoline-1-oxide included squamous cell carcinomas and papillomas; lymphatic tumors and proliferative conditions of the blood were produced less commonly. In addition to producing tumors when administered to living animals, it was also noted that 4-nitroquinoline-1-oxide induces cell transformation *in vitro*. (References).

- 1747 DANGER THROUGH CARCINOGENIC SUBSTANCES IN THE ENVIRONMENT. (Ger.) Gräf, W. (Inst. Hyg., U. Erlangen-Nuremberg, Germany). *Oeff Gesundheitswesen* 33(3):121-133, 1971.

Over 600 substances suspected of being carcinogenic are classified under chemical carcinogens: polycyclic aromatic hydrocarbons, aromatic amines, alkylating agents, nitrosamines, urethane, inorganic chemical poisons, high polymers, natural carcinogens, and cocarcinogens. The occurrence of these substances in our environment may be attributed to substances used in industry, air and water pollution, and naturally occurring substances in plant life. The carcinogenic properties of mycotoxin are described with special reference to the damage such fungi can cause when ingested in animal food mixtures. The nitrites may be used as preservatives for meat or vegetables and may also be found in the intestinal tract through bacterial reduction of nitrates in drinking water. Secondary amines may be produced in cooking or be traced to fish meal used in animal food. The polycyclic aromatic hydrocarbons are a product of our civiliza-

tion and include components of combustion and exhausts and smoke. In addition, these agents are found in nature, and the natural occurrence of benzo(a)pyrene and its effects on men and animals are reviewed (21 references)

- 1748 LUNG TUMORS OF PRIMATES AND RODENTS. (E.) Schepers, G. W. H. (no affil). *Indust Med Surg* 40(1):48-53, 1971.

In the first article in a 3-part series, a survey of 330 cases of human lung cancer observed over a 30-year period was reviewed; most of the cases were associated with exposure to some industrial carcinogen. In addition, lung tumors induced in animal by exposure to industrially significant substances were described. Proven industrial carcinogens included asbestos, nickel, soot, and chromium, and suspected carcinogens included beryllium, engine exhaust, tar fumes and mustard gas. High-risk industries included asbestos mining and manufacturing (prevalences of 32.7 and 51.3 per thousand, resp.), coal mining, gold mining, hematite mining, foundry work and chemical manufacturing. In a total of 130 experiments on guinea pigs, rats, swine, rabbits and cats, potentially carcinogenic chemicals encountered in industry were administered by tracheal injections. Malignant or premalignant changes in pulmonary tissues were induced in animal by beryllium, cadmium, diatomite, and silica, among other agents. (no references)

- 1749 LUNG TUMORS OF PRIMATES AND RODENTS: PART II. (E.) Schepers, G. W. H. *Indust Med Surg* 40(2):23-31, 1971.

Experiments were described in which monkeys and rodents inhaled putatively carcinogenic agents with which industrial workers might come in contact; the carcinogenicity of these agents for the animal lung included rabbits, guinea pigs, hamsters and rats. Only 6% of animals exposed to aluminum aerosols developed alveolar epithelialization and none developed pulmonary tumors. Quartz dust aerosols produced pulmonary lesions in 84% of animals, but produced alveolar epithelialization in only 2.3%. Two animals in the quartz aerosol group developed squamous carcinoma. Submicron amorphous silica compounds were less pathogenic than quartz dust; 67% of animals exposed to these particles developed lesions. Fibrous siliceous aerosols were less pathogenic than crystalline-free silica or submicron amorphous silica aerosols. 42% of the animals developed aerosols in this experimental group. Inhalation of beryllium salts produced lesions in 43% of the animals, alveolar epithelialization in 43% of the animals and lung tumors in 10% of the animals. Also tested were "miscellaneous aerosols", including oil smoke, chalcedony, diatomite, mineral oil, iron chloride and hematite. Lung tumors were seen in less than 0.3% of animals exposed to miscellaneous aerosols. Beryllium aerosol-induced tumors were readily transplanted to other animals through 5 generations of the same species. (no references)

(1750-1760)

- 1750 LUNG TUMORS OF PRIMATES AND RODENTS: PART III. (E.) Schepers, G. W. H. (no affil) *Industr Med Surg* 40(3):8-26, 1971.

The morphology of lung tumors induced in animals by administration of a wide variety of substances potentially dangerous to industrial workers was described. Among so-called "adenomatoid" carcinomata, the most malignant was the acinoid type, which metastasized frequently to the kidney. Other types of adenomatoid tumors were the papilligeroid, circinoid and mucigeroid; these types of tumor were composed primarily of cuboidal cells, columnar cells and goblet cells, respectively. Adenomatoid carcinomas were often induced in rats by inhalation of beryllium aerosols. Epidermoid pulmonary tumors were also seen; some were designated desquamative and some multilayered. Mesotheloid and lymphomatoid tumors were also seen. Among preneoplastic conditions observed in the lung tissue of animals exposed to carcinogens were alveolar epithelialization, bronchiolar epithelial plaque metaplasia, granulomatosis, lymphoid hyperplasia and pleural plaque formation. Whereas no clear morphological differences existed between benign and malignant animal lung tumors, it was noted that human tumors usually allow malignant-benign classification. A second major difference between human and animal tumors was the paucity of mesodermoid lesions in animals. Finally, while human tumors were known to arise frequently in the bronchi, animal lung tumors were found to originate more often in the lung parenchyma. (no references)

- 1751 ENDOCRINE CHARACTERIZATION OF MAMMARY CARINOMAS. (Ger.) Görlich, M. (German Acad. Sci., Berlin). *Arch Geschwulstforsch* 26(4): 385-393, 1970. (24 references)

- 1752 THE ONCOGENICITY OF VIRUSES OF THE HERPES GROUP. (Ger.) Zur Hausen, H. (Inst. Virol., Wurzburg, Germany). *Ber Phys Med Ges Wurzburg* 79: 131-136, 1971. (20 references)

- 1753 THE PHILADELPHIA CHROMOSOME. (Ger.) Merker, H. (Freiburg, Germany). *Deutsch Med Wschr* 96(7):296-298, 1971. (8 references)

- 1754 TUMOR ANTIGENS AND IMMUNE CONTRA-TUMOR REACTIONS. (Ger.) Trepel, F. (Dept. Clin. Physiol., U. Ulm, Germany). *Med Klin* 66(7):215-222, 1971. (54 references)

- 1755 GENITAL HERPES AND CANCER OF THE CERVIX. (Fin.) Leinikki, P. (no affil) and A. Vaheri. *Duodecim* 87(3):181-183, 1971. (no references)

- 1756 CYTOGENETICS AND NEOPLASIA. (Sp.) Ballesta, F. (no affil) and A. Baldellou. *Bol Soc Catalana Pediat* 31(145):240-249, 1970. (42 references)

- 1757 ETIOLOGY AND PATHOGENESIS OF MAMMARY GLAND CARCINOMA. (Sp.) Lozano, R. (Fac. Med. Zaragoza, Spain) and J. Baselga. *Cir Esp* 24(1):1-6, 1970. (no references)

- 1758 ANTIGENIC EXPRESSION OF TUMOR CELLS. (E.) Apffel, C. A. (Pondville Hosp., Walpole, Mass.), J. H. Peters and J. E. Walker. *Boll Ist Sieroter Milan* 49(5):434-447, 1970. (53 references)

- 1759 THE HERPES VIRUS SPECIES. (Fr.) DeRudder, J. (Inst. Pasteur, Paris, France) and D. Lando. *Bull Inst Pasteur* 69(1):7-58, 1971. (163 references)

- 1760 PATHOGENESIS OF LYMPHOPROLIFERATIVE DISEASES INVOLVING IMMUNOLOGICAL DISORDERS. (It.) Ponzzone, A. (Inst. Puericult., U. Turin, Italy), R. P. Tarocco and P. Nicola. *Minerva Pediat* 22(51):2542-2560, 1970. (218 references)

- 1761 INDUCTION OF LUNG ADENOMAS BY CHRONIC INHALATION OF BIS(CHLOROMETHYL) ETHER.
(E.) Leong, B. K. J. (Biochem. Res. Lab., Dow Chem. Co., Midland, Mich.), H. N. Macfarland and H. W. Reese, Jr. *Arch Environ Health* 22(6):663-666, 1971.

Male mice of the A/Heston strain were exposed for 82 and 101 days to bis(chloromethyl) ether (B-CME) or chloromethyl methyl ether (CMME), resp.; B-CME and CMME were introduced to the rats via an aerosol containing B-CME in concentrations of 1 ppm and CMME in concentrations of 2 ppm. Control rats were exposed to untreated air or to an urethan aerosol (138 ppm) for 130 days. The incidence of lung adenomas in the B-CME and CMME groups was 55 and 50% resp., and the average number of tumors per tumor-bearing animal in these 2 groups was 5.2 and 3.1, resp. The incidence of adenomas in the urethan group was 94% vs 41% for untreated controls, and the number of tumors per tumor-bearing animal in the urethan group was 57.5 vs 2.2 in untreated controls. B-CME caused loss of body weight and respiratory distress, but CMME caused no adverse effects. CMME and B-CME were thought to be potentially dangerous agents for industrial workers.

- 1762 MECHANISM OF CARCINOGENESIS WITH 1-ARYL-3,3-DIALKYL-TRIAZENES: III. *IN VIVO* METHYLATION OF RNA AND DNA WITH 1-PHENYL-3,3-[¹⁴C]-DIMETHYLTRIAZENE. (E.) Krüger, F. W. (German Cancer Res. Ctr., Heidelberg), R. Preussman and N. Niepelt. *Biochem Pharmacol* 20(3):529-533, 1971.

Thirty-four male Sprague-Dawley rats were injected i.p. with 0.1 ml/100 g body wt of 1-phenyl-3,3-¹⁴C dimethyltriazene and were killed 9.5 hr after treatment; RNA and DNA were prepared from the pooled organs. 7-Methylguanine was formed in the RNA of all tissues investigated and was also found to be present in the DNA of the liver. These results show that the carcinogen is metabolized in mammals to form an alkylating agent.

- 1763 POTENTIALLY CARCINOGENIC CYCLOPENTA[a]PHENANTHRENES: V. SYNTHESIS OF 15,16-DIHYDRO-7-METHYLCYCLOPENTA[a]PHENANTHREN-17-ONE. (E.) Coombs, M. M. (Imp. Cancer Res. Fund, London, England) and S. B. Jaitly. *J Chem Soc* 1971(2): 230-234, 1971.

Treatment of a 2-acetyl-3-methylnaphthalene furfurylidene derivative with acid was used to prepare 7-[2-(3-methylnaphthyl)]-4,7-dioxoheptanoic acid which was then treated with base; this treatment produced a high yield of a cyclopentenone which absorbed at 259 nm and readily underwent cyclization when boiled with acetic anhydride to give a high yield of 11-acetoxy-15,16-dihydro-7-methylcyclopenta[a]phenanthren-17-one. The parent phenol was prepared from the compound and reduced with sodium in liquid ammonia-tetrahydrofuran to furnish the required 15,16-dihydro-7-methylcyclopenta[a]phenanthren-17-one in 43% yield. The ultraviolet absorption and n.m.r. spectra were compatible with the assigned structure of the product.

- 1764 THE ONCOGENICITY OF N-7-HYDROXYLATED PURINE DERIVATIVES: 7-HYDROXYTHEOPHYLLINE. (Ger.) Guttner, J. (Inst. Microbiol. Exp. Ther., German Acad. Sci., Jena), M. Horn and W. Jungstand. *Arzneimittelforschung* 21(3):356-358, 1971.

Male and female 6-7 wk-old AB/J inbred mice were injected s.c. at 1-wk intervals for 25 wk with 0.7 mg and 1.4 mg of 7-hydroxytheophylline in normal saline and were observed thereafter up to 2 years. Since no dosage-effect relationship was apparent, results from both dose levels were combined. Autopsy findings and histological examinations disclosed that treatment with 7-hydroxytheophylline resulted in approximately 40% more cases of amyloidosis in both sexes than in control animals. No significant difference in mortality was found between controls and treated animals in reticulosarcoma and lung adenoma occurrence. Although no specific carcinogenic effect of 7-hydroxytheophylline could be demonstrated statistically, administration of the agent resulted in a shorter induction time for reticulosarcomas and lung adenomas in females as well as an increased incidence of these tumors in the second half of the animals' life span. This result is in agreement with the carcinogenic effect of this substance described in a previous report on sebaceous gland atrophy tests.

- 1765 CARCINOGENIC EFFECTS OF CYCASIN IN SYRIAN GOLDEN HAMSTERS AND THE TRANSPLANTABILITY OF INDUCED TUMORS. (E.) Hirono, I. (Gifu U. Sch. Med., Japan), K. Hayashi, H. Mori and T. Miwa. *Cancer Res* 31(3):283-287, 1971.

Newborn hamsters given a single s.c. injection of 0.2-0.6 mg cycasin/g body wt developed liver cell adenomas in 5.0% of cases, hepatocellular carcinomas in 8-9% of cases, and intrahepatic bile duct carcinoma in 8-14% of cases. Adult hamsters given a single intragastric dose of 0.15 or 0.1 mg cycasin/g body wt by stomach tube developed liver cell adenomas in 4-5% of cases, no hepatocellular carcinomas, and intrahepatic bile duct carcinomas in 11-22% of cases. Adult hamsters given 2, 3 and 4 administrations of 0.1 mg cycasin/g body wt at 1 month intervals developed liver cell adenomas in 11% of cases (56% of the hamsters given 4 doses of cycasin died within 10-60 days), no hepatocellular carcinomas, and intrahepatic bile duct carcinomas in 9-17% of cases. Eight liver tumors induced by cycasin were transplanted into hamsters, and 5 transplants were successful. Four of the transplantable lines were taken from intrahepatic bile duct carcinomas and 1 was taken from an anaplastic liver cell carcinoma. Hamsters given cycasin also developed gall bladder carcinomas, kidney tumors, intestinal tumors and malignant lymphoma but these lesions were rare.

- 1766 CHROMOSOMAL MUTATIONS BY AZATHIOPRINE IN HUMAN LEUKOCYTES *IN VITRO*. (Ger.) Hampel, K. E. (Med. Clin., Polyclin., Free U. Berlin, Germany), A. Lackner, G. Schulz and V. Busse. *Z Gastroent* 9(1): 47-51, 1971.

azathioprine and 6-mercaptopurine in various solvent media were added to cultures of human peripheral leukocytes to test whether these agents induce chromosomal mutations *in vitro*. Expressed as % metaphases with chromosomal mutations, azathioprine (0.01 mg/ml) in "oximazon" or in butanol induced, resp., mutation values of 60-73% and 12-19%, both significantly greater than controls (0-3%). Addition of 0.1 ml of plasma taken from rats 1 hr after treatment with 125 mg/kg azathioprine i.v. to leukocyte cultures also showed significantly increased values (12-14%), as did a homogenate of the commercial tablet form of azathioprine, murel (0.007 mg/ml) and 6-mercaptopurine (0.006 mg/ml) both in "oximazon" (31-48% and 20-28%, resp.). When test substances were dissolved either in water (pH 8), acetone or polyethylene glycol, the values obtained were not significantly above control levels, indicating that these solvents, unlike "oximazon", do not facilitate cell wall permeation; "oximazon" alone did not induce significant chromosomal mutations in leukocyte cultures.

767 CARCINOGENIC EFFECTS OF 3,3'-DICHLORO-4,4'-DIAMINO-DIPHENYL ETHER IN RATS. (Ger.) Steinhoff, D. (Inst. Exp. Path., Farbenfabriken Bayer AG, Wuppertal-Elberfeld, Germany) and E. Grundmann. *Naturwissenschaften* 57(12):676, 1970.

Forty Wistar rats (20 males and 20 females) were injected s.c. with 3,3'-dichloro-4,4'-diaminodiphenyl ether (250-1000 mg/kg) once weekly (or at longer intervals for the higher doses) for 190 days and a total dose of 10.5 g/kg. Thirty-seven rats which died by day 300 had developed a total of 65 malignant and 2 benign tumors. There were 1 auditory canal carcinomas, and the remaining tumors were not localized in any specific organ; no liver tumors were observed. The longest survival period for treated rats was 545 days. Only 1 of 50 control rats had died at this time and no tumors were found in these animals.

768 INCREASED TUMOR INCIDENCE-RATE IN RATS AFTER INHALATION OF A HIGH-POLYMERIC, WATER-SOLUBLE, SYNTHETIC SUBSTANCE. (Ger.) Weller, H. (Med. Dept., Silicosis Res. Inst., Mining Assoc., Bochum, Germany). *Z Ges Exp Med* 154(3):235-246, 1971.

Prague-Dawley rats were treated with inhalation of an aerosol of poly-2-vinylpyridine-N-oxide (PVNO) in a concentration of 75 mg m⁻³ after dusting or without dust for 20 or 180 min for 5 days/wk for 18 months. Other rats were exposed to aluminum chloride aerosol with and without dust; control rats were treated to dust inhalation or were untreated. Thirteen percent of rats inhaling PVNO developed tumors, while 2.7% of all groups not inhaling PVNO developed tumors. PVNO-treated animals developed a large number of lung tumors, usually more than 1 tumor per animal, as well as tumors in other areas including skin, liver and esentery. Tumor incidence in rats inhaling PVNO only for 180 min/day was 7.9%.

1769 THE EFFECT OF CHRONIC ESTROGENIC STIMULATION ON THE SQUIRREL MONKEY CERVICAL EPITHELIUM. (E.) Graham, C. E. (Yerkes Reg. Primate Res. Ctr., Emory U., Atlanta, Ga.) and S. L. Manocha. *Virchow Arch Zellpath* 7(2-3):147-156, 1971.

Changes in the cervical epithelium of the squirrel monkey were observed in animals given s.c. implanted pellets of estradiol benzoate and cholesterol (1-3 months) or diethylstilbestrol (13-14 months) in concentrations ranging from 10% estradiol and 90% cholesterol to 95% estradiol and 5% cholesterol. Pellets were implanted in the monkeys' thighs or in their backs. Controls treated with cholesterol only were given injections of 0.023 mg estradiol benzoate for 3 days starting 5 days before sacrifice. In controls, the stratified squamous epithelium of the vagina and cervix proliferated and thickened, and the squamocolumnar junction became abrupt. The same effects were produced in monkeys given implanted pellets containing 10 or 95% estradiol; but the thickening of the stratified epithelium was considerable. Monkeys given implanted pellets of 100% diethylstilbestrol for periods of 5 or more months showed several small isolated foci of partially cornified stratified epithelium; the size of these foci varied, and the larger ones penetrated the columnar epithelium and underwent desquamation into the lumen. These foci of stratified cells were seen only rarely in monkeys given 10-95% estradiol. Most of the foci of squamous cells anastomosed to form a reticulum continuous with the main mass of the cervical squamous epithelium. Apparently, the new squamous cells arose by outgrowth from the stratified squamous epithelium at the squamocolumnar junction rather than by squamous metaplasia of columnar cells. The glycogen content was most prominent in the intermediate layer of the cervical stratified epithelium and was depleted after treatment with diethylstilbestrol. The activity of phosphorylases and alcohol dehydrogenase was enhanced in estrogen-stimulated animals.

1770 NUCLEIC ACID METABOLISM OF AN ESTROGEN-DEPENDENT CARCINOMA OF THE ADRENAL CORTEX OF THE RAT. (E.) Redman, L. W. (Cancer Res. Ctr., U. British Columbia, Vancouver, Canada), M. R. Garland, M. Thompson, T. Ng and J. F. Richards. *Cancer Res* 31(3):265-269, 1971.

Young rats were given s.c. implants of an estrogen-dependent adrenal tumor and estrone-containing pellets (90% estrone and 10% cholesterol). By 5-7 days after removal of the estrone pellet, the dimensions of the tumors had decreased. In tumors deprived of exogenous estrogen stimulation and allowed to regress for 3-14 days, the incorporation of ¹⁴C-formate or ³H-cytidine into DNA had decreased to 5-30% of the incorporation rate seen in actively growing tumors. In rats which were restimulated by implantation of new estrone pellets or by an injection of estradiol, the incorporation of precursors into DNA recovered; 24 hr after the reimplantation of estrone pellets, incorporation of precursors into DNA was at 29.6% of the rate found in growing tumors, and incorporation of precursors into RNA was at 81% of the rate seen in

growing tumors. By 18 days after repelleting, incorporation into DNA was 90.3% of that in growing tumors. Nuclear RNA was labeled more rapidly than cytoplasmic RNA in regressing tumors than in growing tumors, suggesting that estrogen may play a role in the transport of RNA from the nucleus to the cytoplasm.

- 1771 EXCRETION OF CYCLOHEXYLAMINE, A METABOLITE OF CYCLAMATE, IN HUMAN URINE. (E.) Asahina, M. (Nat'l. Inst. Hyg. Sci., Tokyo, Japan), T. Yamaha, K. Watanabe and G. Sarrazin. *Chem Pharm Bull* 19(3): 628-632, 1971.

Five normal and 1 diabetic volunteer were given 2 g of sodium cyclamate (CHS-Na) in a single dose, after which 24 hr urine specimens were assayed over 5 days for the presence of CHS-Na and cyclohexylamine (CHA). In 3 cases, most of the CHS-Na (e.g., about 1.5 g) was excreted on the first day; 2 persons excreted maximum amounts of CHS-Na on day 2. Two of the subjects did not excrete appreciable amounts of CHA, while the other 3 excreted between 0.4-0.8 g of CHA from day 2 to day 5. Approximately 33-81% of the ingested CHS-Na as such and 1-18% as CHA were recovered from the urine of subjects. In a related experiment, urinary excretion of CHS-Na and CHA was monitored in 50 volunteers (49 men, 1 woman) eating normal meals during a 2 month period; cyclamate was found in the urine of all volunteers in amounts ranging from 1-700 mg/day. Forty-three of the volunteers excreted CHA, 9 of them more than 10 mg.

- 1772 CHANGES OF STABILITY AND CONFORMATION OF DNA FOLLOWING THE COVALENT BINDING OF A CARCINOGEN. (E.) Fuchs, R. (Ctr. Res. Macromolecules, Strasbourg, France) and M. Daune. *FEBS Letters* 14(4): 206-208, 1971.

Native calf-thymus DNA was reacted with N-acetoxy-acetylaminofluorene and analyzed for melting profiles. Melting curves for the modified DNA obtained at 305 nm in which 31% of the total guanine had reacted with carcinogen revealed a linear increase in temperature at a rate of 1° C/min. The T_m at 260 nm and 305 nm decreased linearly with the amount of modified guanine; the T_m value at 260 nm was always lower than at 305 nm. Extrapolation of the curves to 100% of reacted guanines gave T_m of DNA consisting only of A-T pairs. It is likely that the carcinogen reacts preferentially with G-C rich regions of DNA.

- 1773 REACTIVITIES OF THE CARCINOGENS, N-HYDROXY-2-FLUORENYLACETAMIDE AND N-HYDROXY-3-FLUORENYLACETAMIDE, WITH TISSUE NUCLEOPHILES. (E.) Zieve, F. J. (VA Hosp., Minneapolis, Minn.) and H. R. Gutmann. *Cancer Res* 31(4):471-476, 1971.

Yeast tRNA was incubated with labeled N-hydroxy-2-fluorenylacetamide (or N-hydroxy-3-fluorenylacetamide) and soluble proteins from rat liver for 1 hr; the tRNA was extracted and assayed as the K^+ salt.

The data indicated that the unpurified soluble fraction of rat liver as well as unpurified tRNA from yeast contained low-molecular-wt compounds that inhibited the binding of N-hydroxy-2-fluorenylacetamide; purification of the tRNA increased the binding 25%. Comparison of the N-hydroxy-2-fluorenylacetamide with the N-hydroxy-3-fluorenylacetamide gave values of 3.36 and 4.66 compared to values of 0.23 and 0.08 nanoatoms ^{14}C or 3H bound/mg tRNA, resp., with a slight decrease in values with the addition of tRNA for both compounds. A slight decrease in binding values was seen with the addition of cofactors and tRNA for the first compound and a slight increase for the second compound. Since esterification of N-hydroxy-3-fluorenylacetamide to the sulfate was not accomplished (or the sulfate is unreactive) the question remains whether esterification to a sulfate is the molecular mechanism of the carcinogenic actions of this compound.

- 1774 THE REACTION OF THE CARCINOGEN N-ACETOXY-2-ACETYLAMINOFLUORENE WITH DNA AND OTHER POLYNUCLEOTIDES AND ITS STEREOCHEMICAL IMPLICATIONS. (E.) Kapuler, A. M. (Inst. Physico-Chem. Biol., Paris, France) and A. M. Michelson. *Biochim Biophys Acta* 232(3):436-450, 1971.

The reaction of N-acetoxy-2-acetylaminofluorene (AAAF) with guanosine, deoxyguanosine, adenosine and *Micrococcus lysodeikticus* DNA was studied by spectroscopic and chromatographic techniques. Methods for quantitation of guanosine-AAF, deoxyguanosine-AAF and other nucleotide-AAF complexes are described. The native DNA reacted more rapidly with AAAF than the synthetic ribo- and deoxyribopolynucleotide complexes by a factor of 10; double-helical homopolynucleotide complexes reacted less readily than single-stranded polymers. Reaction of AAAF with DNA occurred at both adenosine and guanosine residues, although adenosine residues in homopolymer double-helical complexes were resistant. This finding suggests that reaction of AAAF in DNA first occurs at guanosine residues followed by adenosine residues in the vicinity. Studies of static models of DNA predict that C-8 of purine residues will be protected from chemical reaction by virtue of its relative inaccessibility due to the *anti*-conformation and the reactivity of DNA with AAAF implicates a dynamic aspect of the double helix; it is likely that guanosine residues conjugated to AAAF are preferentially in the *syn* rather than the *anti* conformation.

- 1775 THIOACETAMIDE INDUCED CHANGES IN RAT LIVER RNA CONTENT. (Ger.) Kullmann, R. (Path. Inst. U. Freiburg, Germany), G. Kiefer and W. Sandritter. *Beitr Path* 143(1):1-13, 1971.

Cytophotometry was used to examine RNA metabolism in liver cells of rats given 25 mg/kg doses of thioacetamide daily for 8-30 days. RNA concentrations in the center of the liver lobule or its periphery were comparable to concentrations in untreated rat livers however, total cytoplasmic RNA content in centrally located liver cells of treated rats was reduced.

compared to total RNA content in livers of untreated rats. Peripheral liver cells in treated rats had higher than normal contents of cytoplasmic RNA. The centrally located liver cells appeared to be more affected by thioacetamide than were peripheral cells, and this effect was produced by a blockage of RNA transport out of nucleoli of centrally located cells. The increase in cytoplasmic RNA in peripheral cells may have represented compensation for the blockage of RNA from central cells.

- 1776 MYCOTOXINS OTHER THAN AFLATOXINS: TUMOR-PRODUCING POTENTIAL AND POSSIBLE RELATION TO HUMAN DISEASE. (E.) Louria, D. B. (New Jersey Coll. Med. Dent., Newark), J. K. Smith and G. C. Finkel. *Ann NY Acad Sci* 174(2): 583-591 1970.

The effect of administration of sonicates or supernates of alternaria and *Aspergillus niger* to 4-6-wk-old mice was studied. A statistically significant increase in leukemia resulted among mice so treated, with the highest incidence occurring among those that were inoculated s.c. for alternaria (75%) and those that were force-fed for *Aspergillus niger* (64%). Aflatoxin-like substances were found in cigarette-smoke condensate when studied by thin-layer chromatography and ultraviolet analyses, but these compounds seemed to be less lethal for embryonated eggs than previously identified aflatoxins.

- 1777 ACUTE AFLATOXIN B₁ TOXICITY IN THE MACAQUE AND ITS SIMILARITIES TO REYE'S SYNDROME. (E.) Bourgeois, C. H. (SEATO Med. Project, Bangkok, Thailand), R. C. Shank, R. A. Grossman, D. O. Johnsen, W. L. Wooding and P. Chandavimol. *Lab Invest* 24(3):206-216, 1971.

Macaque monkeys (*Macaca fascicularis*) were fed capsules made up of 0.5, 1.5, 4.5, 13.5 or 40.5 mg/kg of aflatoxin B₁; the aflatoxin had been produced by *A. flavus* isolated from rice eaten by a Thai child who died with Reye's syndrome. The 1.5 mg and under doses of aflatoxin were not fatal to monkeys; however, 1 of 4 monkeys given 4.5 mg and all monkeys given more than 4.5 mg died within 149 hr, with the first deaths occurring 67 hr after aflatoxin treatment. Symptoms included vomiting, anorexia and lethargy. All fatal cases of aflatoxin poisoning showed marked alterations in serum glucose, nonesterified fatty acids, phospholipids and transaminases by 72 hr after treatment. Serum glutamic-oxaloacetic transaminase and serum glutamic-pyruvic transaminase were markedly elevated in fatal cases, as was the level of nonesterified fatty acids. Phospholipids and glucose were decreased 2- and 5-fold, resp., in treated animals. The liver wt of aflatoxin-treated macaques decreased 15% below the wt of control animals, and livers of aflatoxin-treated animals showed fatty degeneration of hepatocytes, decreased liver glycogen, liver cell necrosis and bile duct hyperplasia. Fatty degeneration was also observed in the hearts and kidneys of affected macaques. The similarities between the toxic reactions of the monkeys to aflatoxin and the clinical and metabolic symptoms of children affected with Reye's syndrome was striking.

- 1778 A SUBACUTE EXPOSURE OF BEAGLE DOGS TO AFLATOXIN. (E.) Armbrrecht, B. H. (Bur. Vetr. Med., Beltsville, Md.), J. N. Geleta, W. T. Shalkop and C. G. Durbin. *Toxic Appl Pharmacol* 18(3):579-585, 1971.

Beagle dogs were given 1, 5 or 20 µg/kg of aflatoxin daily, 5 days/wk for 10 wk. Early consequences of 20 µg/kg of aflatoxin feeding included inappetence, yellow-orange urine and icteric serum. Hemoglobin, hematocrit and erythrocyte values were similar in the different dosage groups. Prothrombin time was significantly increased in dogs given 20 µg/kg of aflatoxin compared to dogs in lower dosage groups; Alkaline phosphatase was increased 4-8-fold in the 20 µg/kg group compared to untreated controls and lower dosage groups. α₂-Globulin and β₂-globulin were decreased in the high aflatoxin dosage group compared to the control and low dosage groups. In livers of the group of dogs given 20 µg/kg aflatoxin there were moderate bile duct proliferation, bile pigment accumulation in the portal areas and multiple vascular channels around the central and portal veins.

- 1779 TERATOGENIC ACTION OF AFLATOXIN B₁, PALMOTOXIN B₀ AND PALMOTOXIN G₀ ON THE CHICK EMBRYO. (E.) Bassir, O. (Dept. Biochem., U. Ibadan, Nigeria) and A. Adekunle. *J Path* 102(1):49-51, 1970.

Aflatoxin B₁, palmotoxin B₀ and palmotoxin G₀ were each injected into the yolk-sac of chick embryos; the dosage of aflatoxin B₁ and palmotoxin B₀ was 0.2-0.6 µg, while the dosage of palmotoxin G₀ was 2.0-6.3 µg. Palmotoxin B₀ produced malformations of the beak and skull, while aflatoxin B₁ induced malformations of the limbs, especially abnormal twisting of limbs; similar results were noted in some chicks hatching from eggs injected with palmotoxin B₀. Other effects of these 2 agents included enlargement and pallor of the liver and retardation of growth. Palmotoxin G₀ administered in amounts of 0.2-1.5 µg produced no obvious ill effects; higher doses induced 14-21% abnormal embryos, as compared to 83-94% abnormal embryos induced by palmotoxin B₀, and 65-90% abnormal embryos produced by aflatoxin B₁.

- 1780 HISTOCHEMICAL HEPATIC CHANGES IN RATS WITH ACUTE AFLATOXIN INTOXICATION. (Fr.) Lageron, A. (Hosp. St. Antoine, Paris, France), W. Schwarzmann and J. Caroli. *Rev Medicochir Mal Foie* 46(1):33-37, 1971.

Crystalline aflatoxin B₁ in dimethylsulfoxide given in a single dose (7 mg/kg) by gavage to male Wistar rats, showed histochemical hepatocellular changes measured at 4 intervals from 4-72 hr. In the cytoplasm, the most important change was the marked reduction of glycogen in periportal hepatocytes. There was a reduction in the activities of glucose-6-phosphate dehydrogenase and in 6-phosphoglucose dehydrogenase which then returned to normal levels in 72 hr; RNA remained slightly diminished through this period. Mitochondrial nicotinamide-adenine-dinucleotide-phosphate-tetrazolium-reductase, ATPase,

isocitrate dehydrogenase, and glutamate dehydrogenase as well as glucose-6-phosphatase of the endoplasmic reticulum all showed persistently decreased activity. In lysosomes there was a rise in β -glucuronidase activity, while acid phosphatase showed a decrease, followed by a rise.

- 1781 IS AFLATOXIN CARCINOGENIC IN MAN? THE EVIDENCE IN SWAZILAND. (E.) Keen, P. (South African Inst. Med. Res., Johannesburg) and P. Martin. *Trop Geogr Med* 23(1):44-53, 1971.

An investigation of the incidence of primary liver cancer in Swaziland indicated that 11 of 90 cases reported between 1964-1968 occurred in the "highveld" area of the country (the western third), 34 cases occurred in the "middleveld" (the central third) and 44 cases occurred in the "lowveld" (the eastern third). These figures yielded risks for populations in the highveld, middleveld and lowveld of 1.0, 1.8 and 4.5, resp., for developing hepatic carcinoma. The condition was more common among Shangaan immigrants than among Swazi tribesmen living in the same areas. The content of the aflatoxin-producing fungus *Aspergillus flavus* in groundnuts from various parts of Swaziland was found to have the same distribution as liver cancer incidence; 20% of groundnuts sampled contained aflatoxin in the highveld, 57% contained aflatoxin in the middleveld, and 60% contained aflatoxin in the lowveld. While groundnuts are eaten by inhabitants in all parts of Swaziland, it was found that in areas of widespread liver cancer, groundnuts were prepared and stored in such a way as to conduce to the infestation of the groundnuts by *A. flavus*. Furthermore, Shangaan tribesmen, who have a high incidence of liver cancer were found to eat groundnuts more regularly than Swazi tribesmen, who have a relatively low incidence of liver cancer. While the findings clearly suggested that aflatoxin was related to liver cancer in Swaziland, the aflatoxin hypothesis could not be extended abroad to account for the incidence of liver cancer in other parts of the world.

- 1782 MITOTIC RATES OF REGENERATING LIVER PARENCHYMA AND DAB INDUCED PRIMARY HEPATOMA. (E.) Bertalanffy, F. D. (Fac. Med. U. Manitoba, Winnipeg, Canada), J. C. W. Parrott and M. L. Ozohan. *Acta Anat* 77(2):216-237, 1970.

The 6-hr mitotic rate of the liver of normal intact rats was $0.02 \pm 0.02\%$; after excision of 70% of the liver, the mitotic rate of parenchyma cells remained at near normal levels until 24-30 hr after hepatectomy, at which time it increased to 0.70% at 30 hr and to a maximum value of 16.0% at 36 hr. After attaining maximum values, the mitotic rate in the parenchyma of hepatectomized rats declined, reaching zero by 8 days after hepatectomy. Mitotic activity in partially hepatectomized rats fluctuated during the day, and was highest during daylight hours and lowest at night. When mitotic rates were determined for the livers of parabiotically joined rats following partial hepatectomy of 1 of them, it was found that hepatectomy of 1 rat augmented the mitotic rate in the intact liver of its parabiotic twin. Hepatomas induced in

rats by chronic feeding with 0.06% preparations of 4-dimethylaminoazobenzene manifested diverse levels of mitotic activity, mitotic rates ranging from 1.63-10.85% in this group. Daily mitotic rates for grade II hepatomas were 19%, and 29% for grades III-IV hepatomas. Mice given implants of the transplantable mouse hepatoma BW7756 showed mitotic rates of 28 and 31% approximately 28-35 days following tumor transplantation.

- 1783 THE ACUTE EFFECT OF AMINOAZOBENZENE AND SOME OF ITS DERIVATIVES ON RNA POLYMERASE ACTIVITY IN ISOLATED RAT LIVER NUCLEI. (E.) Wu, S. Y. (Dept. Path., U. Washington, Seattle) and E. A. Smuckler. *Cancer Res* 31(3):239-247, 1971.

Male rats were given aminoazobenzene (AB), N,N-dimethyl-4-aminoazobenzene (DAB), 2-methyl-N,N-dimethyl-4-aminoazobenzene (2-me-DAB), or 3'-methyl-N,N-dimethyl-4-aminoazobenzene (3'me-DAB) in amounts of 300 mg/kg via gastric intubation, and the capacity of liver cell nuclei to form RNA was observed by measuring tritiated uridine triphosphate (UTP) incorporation into liver cell nuclei. UTP incorporation was enhanced when measured in nuclei isolated from rats treated with DAB or AB; the former agent produced maximal incorporation levels at 24 hr after treatment (4720 cpm/0.1 mg DNA), and AB was maximally stimulatory after 12 hr (4180 cpm). DAB produced a more pronounced and sustained stimulation of UTP incorporation than the other agents. After 48-72 hr after carcinogen treatment, UTP incorporation levels returned to those seen in untreated controls. Rats given repeated doses of DAB showed further potentiation of UTP incorporation. Increased endogenous polymerase activity of liver chromatin was found following azo dye treatment and was maximal following DAB; increased polymerase activity in liver chromatin was also produced by AB. The RNA-polymerase enhancing effects of azo dye treatment may have been due to the carcinogenic transformation effected by azo dyes, or may have been due to the toxicity of the dyes, resulting in alterations of genetic expression.

- 1784 LYSOSOMES OF RAT LIVER AND DAB CARCINOGENESIS. (E.) Takano, T. (Fac. Pharm. Sci., U. Tokyo, Japan), N. Kato, S. Kunimoto-Miyata, S. Goto, S. Ohkuma, D. Mizuno, T. Kitagawa and T. Yokoyama. *Int J Cancer* 7(2):346-352, 1971.

Rats fed for 40 days with 0.06% 4-dimethylaminoazobenzene (DAB) developed nodules and degenerated cells in their livers. Hepatomas had developed by 90 days after commencement of the DAB regimen. The total activity of RNase in liver lysosomes increased by 50% after DAB feeding commenced. Thereafter, RNase activity remained constant. The lysosomal S/P fraction (the ratio of supernatant and precipitated lysosomal fractions prepared by centrifugation) was determined to investigate the intracellular location of lysosomal enzymes including RNase and β -glucuronidase. The S/P ratio increased 2- or 3-fold with DAB feeding up to day 40 and remained constant thereafter.

- 1785 ULTRASTRUCTURAL CHARACTERISTICS OF HEPATOMAS INDUCED BY AZODYES IN THE WISTAR RAT: II. ELECTRON MICROSCOPY OF THE HEPATOMA N-13 A. (Sp.) Peydro Olaya, A. (Fac. Med. Valencia, Spain). *Med Esp* 64(380):283-311, 1970.

Solid and ascitic transplantable tumors induced in rats by chronic administration of 4-dimethylaminoazobenzene were examined by electron microscopy; the ascitic tumor was found to harbor cytosomes different from inclusions seen in other ascites tumors. These cytosomes may have been produced by the granular endoplasmic reticulum; they were proteinaceous and had a crystalline filamentous structure. The ascites tumors appeared as poorly differentiated ascites hepatomas with cells having lobulated nuclei and large nucleoli. Small spherical mitochondria were common and a granular endoplasmic reticulum with poorly developed vesicular forms and highly developed Golgi apparatus were observed. Abundant cytoplasmic glycogen also characterized these ascites tumors.

- 1786 QUANTITATIVE STUDIES OF EARLY CYTOLOGICAL ALTERATIONS INDUCED IN RAT LIVER BY 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE, AS AFFECTED BY 3-METHYLCHOLANTHRENE. (E.) Harman, J. W. (Dept. Path., U. Coll. Dublin, Ireland). *J Path* 102(2):69-85, 1970.

Experiments with male Wistar rats weighing 120-140 g were initiated by incorporation of dye and/or hydrocarbon into the basal diet ration. At necropsy, the right lobe of the liver, the spleen and both kidneys were excised for microscopic examination. The dyed rats were generally sluggish; they developed diarrhea and their fur was ruffled and contaminated with feces. At necropsy, the liver appeared yellow and faintly mottled without showing necrosis or fibrosis. All other tissues were stained a deep yellow, but were otherwise normal. Within 24 hr after the commencement of dye ingestion, structureless hyaline inclusions were noted. These inclusions were most numerous after dye feeding for 10 days and they became less numerous in the following week. Basophilia of the cytoplasm of all parenchymal cells became less intense soon after appearance of hyaline inclusions. When both dye and hydrocarbon were supplied together, the inclusions were less prominent in the cells of the central zone, whereas the peripheral parenchymal cells became slowly and progressively loaded with the same type of inclusions. Further, the loss of cytoplasmic basophilia in the periportal cells was much more marked. After approximately 10 days there were 3 prominent changes (the 2nd phase): ductule hyperplasia, appearance of "new" cells and development of minute foci of atypical parenchymal cells. Simultaneous feeding of dye and hydrocarbon altered the histological localization of the parenchymal cell lesion to the periphery of the lobules (1st phase) and suppressed the 2nd phase. The results indicated that the topographical location of the early parenchymal lesions was important for induction of later ductule and parenchymal lesions and that the hydrocarbon prevented lesions by modifying the lobular distribution of the early parenchymal reaction.

- 1787 PRESENCE OF DMBA-³H IN THE MOUSE OVARY AND ITS RELATION TO OVARIAN TUMOUR INDUCTION. (E.) Krarup, T. (Finsen Inst., Copenhagen, Denmark) and H. Loft. *Acta Path Microbiol Scand* 79(2):139-149, 1971.

Mice were given i.p. or p.o. doses of ³H-7,12-dimethylbenz(a)anthracene (DMBA) and killed 6 hr, 6 days or 2½ months thereafter; on autopsy, specimens of ovarian tissue as well as other tissues were examined for presence of the labeled carcinogen. In ovaries of mice not given DMBA, the number of small oocytes decreased from 6600 at 22 days of age to 3200 at 3 months of age, while in mice given p.o. DMBA, the number of small oocytes decreased from 5100 on day 1 after treatment to 1000 on day 14. I.P. injection of DMBA produced a more marked decline in number of small oocytes. Fat, ovary, adrenal, liver, muscle and brain tissue were examined for ³H-DMBA; in all tissues the maximum amount of label was found 6 hr after feeding with the carcinogen. The lipid-soluble fractions of tissues usually contained more label than the insoluble fractions, and fat contained more label (8728 cpm/mg) than other tissues, while the brain contained the least (417 cpm/mg). The maximum level of radioactivity in tissues was higher in all cases after i.p. administration of the carcinogen than after p.o. administration. Three unilateral ovarian tumors developed in 3- and 5-month-old animals. Only in liver tissues were lipid-soluble and insoluble fractions of tritium of comparable levels. The carcinogenic effect of DMBA on the mouse ovary appears to be due to the parent hydrocarbon rather than to its metabolic products. This carcinogenic effect seemed to be produced immediately upon the application of the carcinogen and consisted in the destruction of small oocytes which led in turn to neoplastic ovarian development. Prolonged retention of DMBA in the ovary after i.p. injection was thought to have no effect on neoplastic development.

- 1788 EXPERIMENTAL ORAL MALIGNANT LYMPHOMA USING ALVEOLAR SOCKET CARCINOGEN IMPLANTATION. (E.) Mesrobian, A. Z. (Sch. Dent., U. Detroit, Mich.) and G. Shklar. *J. Periodont* 42(2):105-108, 1971.

The mandibular first left molar was extracted from the jaw of 40 male and female hamsters; in 20 animals, the root of the tooth was dipped into a powder preparation of pure 7,12-dimethylbenz(a)anthracene (DMBA) and replaced into its alveolar socket position. Control hamsters were untreated, or had molars extracted and replaced without DMBA treatment. All animals undergoing molar extraction showed inflammation of the jaw in the affected region; by 4 wk after surgery, controls showed diminishing inflammation together with lymphoma development. By 8 and 12 wk after surgery, controls had returned to normal, and DMBA-treated animals had developed malignant lymphoma in the submandibular area. Lymphoma arose in periosteal soft tissue and contained many lymphoblastic cells. Malignant lymphomatous lesions were found within the mandible itself in marrow spaces adjacent to the replanted molar tooth. Two

lymphomatous hamsters also developed invasive epidermoid carcinoma of the submandibular region.

- 1789 EFFECT OF HORMONE STIMULATION, DOSE, AND TIME OF ADMINISTRATION OF CARCINOGEN ON CARCINOGEN-INDUCED MAMMARY TUMORS FROM PRENEOPLASTIC NODULE OUTGROWTHS. (E.) Medina, D. (Baylor Coll. Med., Houston, Tex.). *J Nat Cancer Inst* 46(4):909-916, 1971.

The tumorigenic effects of 7,12-dimethylbenz(a)anthracene (DMBA) and urethan and of γ -irradiation were analyzed on nodule outgrowth line D1, one of a series of BALB/c mouse mammary tumor virus-free outgrowths. DMBA and urethan treatment produced 68% and 83% tumor growth, whereas irradiated outgrowths produced only 23% tumor growths. Hormone stimulation (pituitary isograft) enhanced the effects of DMBA, whereas hormone effects with urethan administration failed to show statistically different results and γ -irradiation was inhibited in its ability to produce tumors. Time of administration and dosage determined the response of outgrowths to urethan; exposure at 3-5 wk after transplantation resulted in greatest incidence of outgrowth. Apparently the nature of the cell population exposed to the carcinogen determined the response of the outgrowths.

- 1790 THE EFFECT OF THYROACTIVE SUBSTANCES ON THE INDUCTION OF CERVICO-VAGINAL AND VULVAL TUMOURS IN CASTRATE RATS AT VARIOUS LEVELS OF CARCINOGENIC TREATMENT. (E.) Glucksmann, A. (Strangeways Res. Lab., Cambridge, England) and C.P. Cherry. *Brit J Cancer* 24(4) 769-784, 1970.

The effect of L-thyroxine and methylthiouracil on thresholds for carcinogenesis of 7,12-dimethylbenz(a)anthracene (DMBA)-induced cervico-vaginal and vulval tumors was studied in castrate hooded rats of the Lister strain by p.o. administration of the thyroactive substances. At 40 paintings of cervix, vagina and introitus with DMBA, dose-response curves show that both methylthiouracil and L-thyroxine make a significant difference in incidence of tumor induction. Sarcomas reached a peak incidence of 25% with 20 doses of carcinogen in nonmedicated rats and rose to 90% with the use of thyroactive drugs. Methylthiouracil accelerated the formation of squamous cell vulval tumors at lower doses of DMBA, while L-thyroxine slowed the rate of tumor induction with longer DMBA treatment. Central regulatory factors must be responsible for the effects of variations in doses of DMBA on carcinogenesis.

- 1791 EFFECTS OF 7,12-DIMETHYLBENZ[a]ANTHRACENE ON RNA POLYMERASE IN ISOLATED MAMMARY GLAND CELL NUCLEI. (E.) Tominaga, T. (Roswell Park Mem. Inst., Buffalo, N. Y.), T. L. Dao and P. R. Libby. *Proc Soc Exp Biol Med* 136(3):694-697, 1971.

Rats of both sexes were fed 20 mg of 7,12-dimethylbenz(a)anthracene(DMBA) on 1, 2 or 4 days prior to killing, and nuclei from mammary gland cells were assayed for Mg^{2+} -activated RNA polymerase, and Mn^{2+} -

$(NH_4)_2SO_4$ -activated RNA polymerase. In male rats enzyme activity values for the DMBA-treated rats were not significantly different from values for untreated controls. No significant changes were found in female rats in the levels of the Mg^{2+} -activated polymerase before and after DMBA treatment. In female rats, the Mn^{2+} -ammonium sulfate-activated enzyme showed inhibition relative to control values at 1 and 2 days after DMBA feeding, and increased thereafter to exceed control values. At 1 day after DMBA feeding Mn^{2+} -ammonium sulfate-activated enzyme levels in control and DMBA-fed rats were, resp., 36.46 and 25.02 μ moles of UTP incorporated into RNA/10 min/mg DNA. At 4 days after DMBA feeding, control and DMBA-fed levels for this enzyme were resp., 34.70 and 46.88 μ moles TUP/10 min/mg.

- 1792 THE EFFECT OF DISTAL SMALL BOWEL BYPASS AND RESECTION ON 7,12-DIMETHYLBENZ[a]ANTHRACENE PRODUCED MAMMARY CARCINOMA IN THE RAT. (E.) Weinberg, M. (Temple U. Hlth. Sci. Ctr., Philadelphia, Pa.), L. Goldman, M. Gruenstein, D. R. Meranze and M. B. Shimm. *J Surg Res* 11(2):101-103, 1971.

Female rats were fed 10 mg of 7,12-dimethylbenz(a)anthracene (DMBA) 1 wk before or after undergoing distal small bowel bypass or resection; in 1 group of rats, distal small bowel bypass was effected 1 wk prior to concomitant administration of DMBA and cholic acid. The wt and serum cholesterol of animals in the various groups were similar. Ninety-two percent of intact control rats given DMBA developed mammary adenocarcinomas. Thirty-seven percent of the rats undergoing distal small bowel bypass followed by DMBA developed tumors, and 97% of the rats given DMBA followed by bypass developed mammary tumors. Sixty-one percent of rats given DMBA prior to resection developed tumors, and 65% of rats given DMBA and cholic acid following bypass developed tumors.

- 1793 TUMOR-PROMOTING ACTIVITY OF TOBACCO EXTRACTS. (E.) Bock, F. G. (Roswell Park Mem. Inst., Orchard Park, N. Y.). *J Indian Med Prof* 17(3):7561-7564, 1970.

Commercial cigarette tobacco was extracted with aqueous barium hydroxide solution and painted on the skin of mice previously treated with a single dose of 125 μ g of 7,12-dimethylbenz(a)anthracene. Mice were given extract from $\frac{1}{2}$ g of tobacco daily. The tobacco extract was seen to have marked tumor promoting effects; the percentage of mice with tumors which had been treated with carcinogen and tobacco extract increased from 12% at wk 10 of extract treatment to 30% by wk 26. In contrast, less than 1% of the mice given carcinogen only had developed tumors by week 26. Attempts to isolate the tumor-promoting agents in the tobacco extracts indicated that 2 agents were at work; one agent had a high molecular wt and was insoluble in methanol and the other had a low molecular wt and was soluble in methanol. The high molecular wt component was thought to be a tobacco pigment. Extracts of cigarettes made by 5 American and 2 British companies produced tumors in 11-44% of mice; the chemicals added to the American cigarettes during manufacture

did not increase tumorigenicity significantly over that of British cigarettes, which are relatively additive-free. The tumor promoting properties of cigarette tobaccos were thought to be due either to chemicals used in growing the tobacco or to chemical changes occurring in the tobacco leaf during the curing and aging of the leaf. Extracts of uncured fresh tobacco leaves raised without chemical insecticides or suckering agents had only weak efficacy as tumor-promoting agents.

1794 THE DEVELOPMENT OF DIMETHYLBENZANTHRACENE-INDUCED MAMMARY GLAND TUMORS IN RATS WITH DIFFERENT HORMONAL CONDITIONS. (Rus.) Turkevich, N. M. (Res. Inst. Exp. and Clin. Oncol. Kiev, U.S.S.R.) and Ya. D. Matveychuk. *Vop Onkol* 17(1): 41-45, 1971.

The development of dimethylbenzanthracene (DMBA)-induced mammary gland tumors under various estrous conditions as affected by daylight hours or by reserpine in white female rats was investigated. Three groups of rats were used: group I was subjected to a 14 day study of vaginal smears before and after reserpine treatment (1 mg/kg s.c. single dose) followed by DMBA (2 mg i.v. 3 times at 6 day intervals) given 2 wk after reserpine; group II underwent a 14 day study of the estrous cycle prior to DMBA administration using dosage as above; in group IIIa, administration of DMBA was followed by an estrous cycle study during the month of August and in group IIIb DMBA administration followed an estrous cycle study during November, January and February. The experimental period lasted 6 months after the last administration of DMBA when 50% of the animals had developed carcinomas of the mammary gland. The rats which developed tumors had 4 estrous days in November while animals which developed no tumors had 7 estrous days. The number of estrous days increased during January and February from 7 to 9 in rats which did not develop tumors and from 4 days to 10 days in animals which developed carcinomas. Reserpine decreased the number of estrous days from 8 to 6 and DMBA reduced the estrous days from 7 to 3 in rats which developed tumors and from 7 days to 6 days in rats which developed no tumors. A direct relationship between the variability of the estrous cycle and DMBA carcinogenesis could be established.

1795 INHIBITION OF MURINE SUBCUTANEOUS AND INTRAVENOUS BENZO(rst)PENTAPHENE. CARCINOGENESIS BY SWEET ORANGE OILS AND d-LIMONENE. (E.) Homburger, F. (Bio-Res. Inst., Cambridge, Mass.), A. Treger and E. Boger. *Oncology* 25(1): 1-10, 1971.

Three groups of 50 male C57BL/6 Jax mice were injected s.c. with 25 µg of benzo(rst)pentaphene (DBP) in 0.1 ml tricapylin and 50 control animals received 0.1 ml of tricapylin alone. Twenty-four hr later, 0.2 ml of one or the other of 2 types of sweet oil of orange was administered s.c. to a group of 50 mice. None of the mice receiving

orange oil alone or tricapylin alone developed tumors in the 2-yr observation period. The tumor appearance rate in animals given DBP alone was twice as high as in animals given DBP and sweet orange oil. When injection sites taken from these mice were transferred into fresh hosts which were given s.c. injections of sweet orange oil 24 hr later, the rate of tumor development was affected in the same manner as in animals administered DBP directly. Of 50 female A/Jax mice injected in the tail vein with DBP alone, 74% developed lung adenomas, while those given DBP and sweet orange oil had an adenoma incidence of 44%. Limonene reduced the DBP tumorigenicity to 40%, while limonene hydroperoxide had less effect and 5-fluorouracil had no effect.

1796 CIGARETTE SMOKE: STIMULATORY EFFECT ON METABOLISM OF 3,4-BENZOPYRENE BY ENZYMES IN RAT LUNG. (E.) Welch, R. M. (Wellcome Res. Lab., Burroughs Wellcome Co., Research Triangle Park, N. C.), A. Loh and A. H. Conney. *Life Sci* 10(4):215-221, 1971.

Female rats were allowed to breathe a mixture of cigarette smoke and air in a smoke-filled chamber for 1-4 hr, and the ability of the lung to hydroxylate 3,4-benzopyrene (BP) was assayed. BP-hydroxylase activity in lung was decreased 27% after 1 hr of exposure to smoke; after 2 and 4 hr of exposure, however, the enzyme activity increased 34% and 186%, resp. Rats not exposed to cigarette smoke showed no change in lung BP-hydroxylase. Actinomycin (2 mg/kg body wt) administered i.p. 30 minutes prior to smoke exposure completely blocked the increase in BP-hydroxylase following smoke exposure. Puromycin administered 1 hr prior to smoke exposure similarly prevented the increase in BP-hydroxylase, indicating that the induction of lung BP-hydroxylase activity by cigarette smoke required the synthesis of RNA and protein. After exposure to smoke for 5 hr/day for 3 days, BP-hydroxylase activity in lung and placenta of pregnant rats was increased 12- and 4-fold, resp. Enzyme inducers in the cigarette smoke may be able to reach the fetus in mothers exposed to smoke.

1797 THE STUDY OF DEVELOPMENT OF LUNG AND SKIN TUMORS IN MICE EXPOSED *IN UTERO* TO POLYCYCLIC HYDROCARBONS. (E.) Bulay, O. M. (Ankara U. Med. Sch., Turkey). *Acta Med Turcica* 7(1):3-38, 1970.

The effect of benzo(a)pyrene (12mg) and 7,12-dimethylbenz(a)anthracene (DMBA, 1-4 mg) on the fetus *in utero* was studied in Swiss Ha/ICR mice that were injected i.p. with carcinogens on the 11th, 13th and 15th days of gestation. In mice delivered by caesarean section, the incidence of pulmonary adenomas in the benzo(a)pyrene group was 71.4%, whereas in animals born spontaneously, the incidence was 58.3%. The tumors attained a diameter of 2-3 mm, were sharply circumscribed and located on the surface and covered by pleura. Skin papillomas resulted in 28.9% of the group treated *in utero* with benzo(a)pyrene and

postnatal croton oil application, compared to the control group treated with croton oil only, in which the incidence was 14.2%. High doses of DMBA with croton oil resulted in the highest percentage of skin papillomas (31.1%). *In utero* carcinogenic effects were produced by transplacental passage of polycyclic hydrocarbons.

- 1798 THE MECHANISM OF CARCINOGENESIS BY THE NEUTRAL FRACTION OF CIGARETTE SMOKE CONDENSATE. (E.) Roe, F.J.C. (Chester Beatty Res. Inst., London, England), R. Peto, F. Kearns and D. Bishop. *Brit J Cancer* 24(4): 788-806, 1970.

The carcinogenic effect of the neutral fraction of smoke condensate on mouse skin was studied in 16 groups of Swiss female SPF mice by application of various combinations of benzo(a)pyrene and the neutral fraction of cigarette smoke in acetone to skin. Treatment 3 times a wk with both agents resulted in the appearance of malignant skin tumors in 114 animals, 28 of which developed more than one tumor and 28 of which showed metastatic deposits. In single-treatments with benzo(a)pyrene a non-linear dose-response curve for carcinogenicity revealed that a single dose produced a rate of cancer incidence greater than twice the rate produced by half that dose, while a linear dose-response curve was obtained with the neutral fraction. However a higher incidence rate than the sum of the incidence rates when used alone was seen in combination. These findings suggest that the neutral fraction acts mainly on only one rate-determining step of the carcinogenic process.

- 1799 HUMAN PLACENTAL HYDROXYLATION OF 3,4-BENZOPYRENE DURING EARLY GESTATION AND AT TERM. (E.) Juchau, M. R. (Sch. Med. U. Washington, Seattle). *Toxic Appl Pharmacol* 18(3):665-675, 1971.

Hydroxylation of benzo(a)pyrene was assayed in placental tissues of women in various stages of pregnancy with differing histories of cigarette smoking; results were compared with benzopyrene hydroxylase (BPOHase) found in placental tissues of pregnant rats injected with 20 mg/kg 3-methylcholanthrene. In humans, readily detectable levels of BPOHase were found only in placental tissues of women who smoked cigarettes at term. In these subjects, the level of placental BPOHase was 70 U/mg protein/hr, while for women at term who did not smoke, placental BPOHase was 4.7 U/mg/hr. Placental BPOHase from women 8-16 wk into pregnancy measured 1.6 U/mg/hr for smokers and less than 0.4 U/mg/hr for nonsmokers. Placentas of rats not given 3-methylcholanthrene showed only minimal BPOHase activity, while placentas from pretreated rats exhibited a 12-fold increase in BPOHase. BPOHase activity in human fetal or neonatal livers was not detectable. Examination of BPOHase values for individual patients indicated that a positive correlation between gestational age and enzyme activity existed, and that a similar correlation existed between number of cigarettes smoked by mothers and placental BPOHase.

- 1800 BENZO(a)PYRENE IN THE WORKPLACE ATMOSPHERE OF COAL AND PITCH COKING PLANTS. (E.)

Masek, V. (Res. Inst. NHKG Steelworks, Ostrava-Kuncice, Czechoslovakia). *J Occup Med* 13(4):193-198, 1971.

Concentrations of benzo(a)pyrene in Czech coal and pitch coking plants were found to be maximal in the immediate vicinity of the pitch battery (3,815 µg/cubic meter of air) and were higher in the winter months than in the summer. Benzo(a)pyrene concentration in the air of the coking plants was determined by collecting filtered air samples and isolating the carcinogen by means of chromatography. Charging the coke ovens by a steam injection technique produced 10% less benzo(a)pyrene pollution than charging the ovens by gravity.

- 1801 INFLUENCE OF *CANDIDA ALBICANS* GLYCOPROTEIN ON 3-METHYLCHOLANTHRENE INDUCED MALIGNANCY IN NEWBORN RODENTS. (E.) Mankowski, Z. T. (Western Inst. Cancer Leukemia Res., Santa Monica, Calif.). *Mycopathologia* 44(2):95-100, 1971.

Newborn rats and albino noninbred mice were given s.c. injections of 166 µg of 3-methylcholanthrene (3-MC)/g body wt (rats) or 25.5 µg of 3-MC/g wt (mice); after weaning, rats and mice were injected 5 times weekly with *Candida albicans* (C.a.) glycoprotein. Animals were given either 9.5 µg or 18.5 µg C.a. glycoprotein. In the 6 months following treatment, rats given only 3-MC developed s.c. tumors in 30% of the cases, rats given 9.5 µg C.a. glycoprotein developed tumors in 65% of the cases, and rats given 18.5 µg C.a. glycoprotein developed tumors in 80% of the cases. Rats given C.a. glycoprotein as well as 3-MC developed tumors earlier than did rats given 3-MC only; 23 tumors were observed in 20 rats given C.a. glycoprotein by 5 months after treatment, and 3 tumors observed in 20 rats given 3-MC only at this time. Tumors developed by rats given C.a. glycoprotein attained larger dimensions than those developed by untreated rats. Similar results were obtained for mice, which developed a high incidence of thymomas when treated with C.a. glycoprotein and 3-MC.

- 1802 SUSCEPTIBILITY OF MAMMARY-TUMOR-VIRUS-FREE BALB/c MOUSE MAMMARY NODULE OUTGROWTH CELLS IN DNA SYNTHESIS TO 3-METHYLCHOLANTHRENE TUMORIGENESIS. (E.) Adamson, R. (Inst. Cell. Res., U. Nebraska Lincoln), M. R. Banerjee and D. Medina. *J Nat Cancer Inst* 46(4):899-907, 1971.

The relationship between the frequency of cells in the proliferative pool during DNA synthesis and the carcinogenic efficiency of 3-methylcholanthrene during the progressive growth of D1 nodule outgrowth tissue following fat-pad transplantation was studied in mammary-tumor-virus-free outgrowths of BALB/c mice by means of thymidine labeling. As measured by ³H-thymidine incorporation, DNA synthesis in the outgrowths gradually increased and reached a peak 4 wk after fat-pad transplantation; the rise in DNA synthesis rate during the initial 3 wk was relatively

slow, and after 4 wk the incorporation of the labeled DNA precursor increased 150% over the value obtained at 1 wk after transplantation; this peak was followed by a consistent drop to 37% at 8 wk. The frequency of labeled alveolar epithelial cells showed a rise and peaked also at 4 wk after transplantation but was reduced at 5 wk and remained constant until the 8th wk. D1 nodule outgrowths in mice receiving 3-methylcholanthrene feedings at 3 and 5 wk after transplantation produced 56% and 67% tumors, resp., in 2 groups; however, later administration of the carcinogen resulted in a decreased incidence of tumor formation as well as a failure of tumors that did form to increase in size between feedings; this differed from observations in animals fed 3-methylcholanthrene at 3 and 5 wk where a 100% increase of outgrowth size occurred during the 2 feedings. Results suggest that an interaction does occur between methylcholanthrene and DNA.

803 CHROMOSOME STUDIES ON A TRANSPLANTABLE GRANULOCYTIC LEUKEMIA (CHLOROLEUKEMIA) OF RAT. (Jap.) Sakai, T. (Showa U. Sch. Med., Tokyo, Japan). *Acta Haemat Jap* 33(4):402-414, 1970.

A granulocytic leukemia of the chloroleukemia type induced by 3-methylcholanthrene in rats was found to have chromosome numbers of 37-44 with 80% of the tumor cells having 43 chromosomes. An extra-long telocentric and a small chromosome were observed in the stemline karyotypes; a distal part of an acrocentric element appeared to have been translocated to 1 of the number 2 acrocentric chromosomes resulting in the extra-long element, while the other part of the acrocentric together with the centromere formed the small element. Cells with 42 or 44 chromosomes, which were occasionally seen, were thought to have been formed by the non-disjunction of one of the number 14 chromosomes. The tumor was found to have infiltrated the femoral bone marrow of tumor-bearing rats; the ratio of tumor cells to bone marrow cells was 10% and increased rapidly after the tumor had attained a size of 20 g. Infiltration by tumor cells of the peritoneal cavity was also seen; in the peritoneal cavity the tumor developed as an ascites tumor in the 47th and 60th transplant generation.

804 THREAD-INDUCED EPIDERMIZATION IN THE UTERINE HORN OF MICE, AND THE INFLUENCE OF 20-METHYLCHOLANTHRENE. (E.) Graham, C.E. (Yerkes Reg. Primate Res. Ctr., Emory U., Atlanta, Ga.). *Oncology* 25(1):83-93, 1971.

The mode of origin of new stratified squamous epithelium in response to implantation of beeswax-impregnated thread into the uterine cornua of C₃H/HeJ mice at the age of 6 wk was studied by means of stereomicroscopy. In animals treated with carcinogen/beeswax impregnated thread, more than 90% developed early invasive lesions of the stratified epithelium of the cervical canal with an abrupt demarcation between the stratified and columnar epithelium; the mean level of the junctions in contact

with the thread was invariably displaced cranially, and in some instances extended the total length of the uterus. In animals implanted with beeswax-impregnated thread without carcinogen the mean cranial displacement of the junction was least, and an intermediate amount of epidermization occurred in animals treated with plain thread. The histological appearance of the original and newly formed epithelium after contact for 4 wk with beeswax and 3-methylcholanthrene threads had a somewhat disorganized appearance, lacked a prickle-cell layer, and the surface layers were neither flattened nor cornified but presented occasional areas of atrophy; upon serial section both control and carcinogen-treated cervixes demonstrated continuity of the new stratified epithelium with the main mass. It appears likely that squamous cell cervical carcinomas arise not from the columnar cells but from stratified epithelium.

1805 ALTERATION IN THE MICROSOMAL HEMOPROTEIN AND THE KINETICS OF 3,4-BENZOPYRENE HYDROXYLASE INDUCED BY 3-METHYLCHOLANTHRENE: TIME COURSE STUDY AND EFFECTS OF PUROMYCIN. (E.) Alvares, A. P. (Rockefeller U., New York, N. Y.), G. Schilling and R. Kuntzman. *Life Sci* 10(3):129-136, 1971.

A dose of 25 mg/kg of 3-methylcholanthrene (MC) dissolved in corn oil was administered by a single i.p. injection to male Sprague Dawley rats. Actinomycin D was administered i.p. 1 hr prior to and 5 hr after the administration of MC. At hourly intervals for 12 hr, rats received puromycin (20 mg/kg, i.p.); rats were killed 1 hr after the last dose. Three and 12 hr after administration of MC, increases occurred in both the V_{max} and the ratio of 455:430 nm peaks of the ethyl isocyanide difference spectra of microsomes with a concurrent decrease in the apparent K_m for the hydroxylation of 3,4-benzopyrene. Puromycin alone had no effect on the apparent K_m of the hydroxylase whereas MC caused a marked decrease. This decrease was prevented when MC administration was followed by hourly injections of puromycin. Similarly, the increase in V_{max} and in the ratio of the 455:430 nm peaks following administration of 3-methylcholanthrene was prevented when followed by injections of puromycin. Similar results were obtained when actinomycin D was substituted for puromycin.

1806 PULMONARY ADENOMATA INDUCED BY CARCINOGEN TREATMENT IN ORGAN CULTURE: INFLUENCE OF INCREASING AMOUNTS OF CARCINOGEN. (E.) Davies, R. F. (Tobacco Res. Council, Harrogate, England), I. R. Major and E. R. Aberdeen. *Brit J Cancer* 24(4):785-787, 1970.

The effects of increasing amounts of tobacco carcinogens on mouse lung cultured *in vitro* was studied in BALB/c mice. Explants examined immediately after treatment in culture whether exposed to carcinogen or not were normal in appearance. However, explants after inoculation into mice showed lymphoid hyperplasia which did not appear to be influenced by the carcinogen or the development of an adenoma. The percentage of

takes with adenomata ranged from 30% with 4.4 µg/ml 3-methylcholanthrene to 64% with 7.1 µg/ml 3-methylcholanthrene.

- 1807 ULTRASTRUCTURAL ANALYSIS OF RENAL MESENCHYMAL TUMOR INDUCED IN THE RAT BY DIMETHYLNITROSAMINE. (E.) Hard, G. C. (Med. Res. Counc. Lab., Carshalton, England) and W. H. Butler. *Cancer Res* 31(3):348-365, 1971.

The predominant cell type in renal mesenchymal tumors induced in rats by injections of dimethylnitrosamine was spindle shaped, but stellate cells were frequent in less cellular areas of the stroma. Tumor cells also differentiated into pericytes, endothelial cells, vascular smooth muscle fiber cells, and rhabdomyoblasts. In the spindle-shaped cells, granular endoplasmic reticulum was conspicuous in the cytoplasm, and ribosomes were numerous. Tumor cells frequently formed small aggregates enclosing a cleft-like lumen; the formation of these groups resembled capillary formation. Tumor cells tended to group together in areas of low cell-density as well as in areas of high cell-density. Enclosed lumina occasionally contained red cells. The tumor areas were supplied with vascular channels which were lined with endothelial cells indistinguishable from adjacent free tumor cells, showing that the vascular-lining cells were an integral part of the tumor. Epithelial tissue consisted of isolated preexisting tubules and glomeruli; some tubules were stimulated to hyperplastic proliferation. Mesenchymal tumor cells could not be shown to be the origin of the epithelial elements. Apparently, the renal mesenchymal tumor should be regarded as a vascular tumor arising from mesenchymal cells in the renal cortical interstitial space.

- 1808 ULTRASTRUCTURAL STUDY OF THE DEVELOPMENT OF INTERSTITIAL LESIONS LEADING TO MESENCHYMAL NEOPLASIA INDUCED IN THE RAT RENAL CORTEX BY DIMETHYLNITROSAMINE (E.) Hard, G. C. (Med. Res. Counc. Lab., Carshalton, England) and W. H. Butler. *Cancer Res* 31(3):337-347, 1971.

Male rats were given i.p. injections of 30, 50 or 60 mg/kg dimethylnitrosamine (DMN) and killed after periods ranging from 1 day to 20 wk later; kidney sections were prepared for electron microscopic examination. Intracellular damage was visible in interstitial fibroblasts in the vicinity of glomeruli within 1 day after injection of DMN; intracellular changes involved accumulation of lipid droplets, formation of myelin figures, disorganization of nucleoli and dilation of the rough endoplasmic reticulum in some cells. By 4 days postinjection, autophagic vacuoles were seen in some cells. Within 2-4 days, some periglomerular cortical fibrocytes and capillary endothelial cells were stimulated into division. Monocyte infiltration through breaks in capillary walls was frequent. An interstitial mononuclear inflammatory reaction with the macrophage as the dominant cell was observed, reaching a peak by 7 days postinjection. By 3 wk postinjection and thereafter, some hypercellular foci persisted, and the lymphocyte was the dominant cell form. By 12 wk,

there was a marked reduction of immunological cells, and persisting lesions consisted chiefly of aggregation of fibroblast-like cells similar to spindle or stellate tumor cells. By 20 wk postinjection, mesenchymal tumors were seen to be well developed and showed wide cellular differentiation. All changes were most pronounced in cells from rats given 60 or 50 mg DMN; in animals given 30 mg DMN, lesions were milder and persisted in only about 30% of cases.

- 1809 ULTRASTRUCTURAL ASPECTS OF RENAL ADENOCARCINOMA INDUCED IN THE RAT BY DIMETHYLNITROSAMINE. (E.) Hard, G. C. (Med. Res. Counc. Lab., Carshalton, England) and W. H. Butler. *Cancer Res* 31(3):366-372, 1971.

Renal tumors were induced in rats by a single i.p. injection of 50 mg/kg dimethylnitrosamine, and examined under the electron microscope. Cells within a single tumor showed widely varying degrees of cytoplasmic differentiation; in well-differentiated cells, mitochondria of circular or elongate outline were common, while in more poorly-differentiated cells the mitochondria were usually of irregular shape. The cells of the adenocarcinomas developed abnormal clusters of brush border, usually at the junction of closely apposed cells. Tumor cells also showed hypertrophied nucleoli and Golgi apparatus. These features of dimethylnitrosamine-induced adenocarcinomas appeared to confirm the hypothesis that these tumors arise from proximal convoluted tubules.

- 1810 RENAL TUMORS INDUCED IN RATS BY DIMETHYLNITROSAMINE: ESPECIALLY ON ITS HISTOGENESIS AND GROWTH PATTERN. (Jap.) Kimura, M. (Sch. Med. Tokushima U., Japan). *Shikoku Acta Med* 26(5):481-489, 1970.

Renal tumors were induced in newborn and adult rats placed on 3 regimens of dimethylnitrosamine (DMN) administration: 1 group of adults was fed a diet containing 200 ppm of DMN for 2 months; a second group consisted of newborn rats which were given a single s.c. injection of 100 µg DMN and 50 ppm of DMN in drinking water; a third group of newborns was given a single s.c. injection of 100 µg DMN. Nonepithelial tumors of the kidney developed in all 3 experimental groups; epithelial tumors developed only in animals in the first group. Nonepithelial tumors were composed chiefly of undifferentiated mesenchymal tumor cells. Tumor nodules composed of spindle-shaped tumor cells were seen at the corticomedullary junction in sections of early kidney lesions. These tumors may have arisen from interstitial cells of the corticomedullary junction to fuse and enlarge. Epithelial renal tumors were adenomas or adenocarcinomas.

- 1811 STUDIES ON THE TRANSPLACENTAL TERATOGENIC, CARCINOGENIC, AND MUTAGENIC EFFECT OF DIMETHYLNITROSAMINE AFTER ORAL ADMINISTRATION TO RAT.

(Ger.) Sydow, G. (German Acad. Sci., Berlin). *Arch Geschwulstforsch* 36(4):331-334, 1970.

Male and female rats aged 5 months were given 1 mg diethylnitrosamine (DENA) per animal in drinking water daily. After 35 days (series A), 50 days (series B) and 60 days (series C), 20 males and females of each group were mated, at which time and until parturition, the animals continued on DENA. The newborn were kept until they died at which time they were examined for tumors. The young of series A, were mated at 5 months without any further treatment with carcinogen and followed for 4 generations or observation of the mutagenic effect of the carcinogen. The oral ingestion of the DENA had no effect on the conception and fertility of the animals; no teratogenic, mutagenic or carcinogenic effects were observed in newborn rats. The life span of the offspring of the treated animals were shortened by about 1 year due to pneumonia or to degenerative inflammation and necrosis of the liver. These pathological changes were not observed in the following generation.

1812 DIETHYLNITROSAMINE-INDUCED RENAL TUMORS IN PARTIALLY HEPATECTOMIZED RATS. (Ger.) Habes, H. (Path. Inst. U. Munich, Germany), R. Harenstein and J. Gminder. *Naturwissenschaften* 58(2):102-103, 1971.

Three groups of partially hepatectomized rats were given a single i.p. injection of 80 mg/kg of diethylnitrosamine (DENA) at 4, 16 or 24 hr after surgery. Six hundred days later, mortalities with renal tumors were 78%, 59% and 20%, resp., for the 3 groups; mortalities increased to 83%, 65% and 53%, resp., by 900 days after surgery. Massive bilateral tumors up to 7 cm in diameter had developed and were comprised of adenomas, adenocarcinomas and anaplastic tumors. However, no hepatic tumors were found. It is postulated that because of the hepatic dysfunction due to partial hepatectomy, the formation of the proximate carcinogens from DENA in the liver was reduced, so that hepatic tumors did not develop; for similar reasons, the biological half-life of the carcinogen increased. As a result there may have been a greater possibility that a critical level of carcinogen required for production of tumors in the kidney was reached.

1813 CARCINOGENIC ACTIVITY OF ALIPHATIC NITROSAMINES VIA THE MOTHER'S MILK IN THE OFFSPRING OF SYRIAN GOLDEN HAMSTERS. (E.) Mohr, U. (Med. Coll. Hannover, Germany) and J. Althoff. *Proc Soc Exp Biol Med* 136(3):1007-1009, 1971.

Female hamsters were given s.c. injections of 5, 10 or 20 mg/kg diethylnitrosamine (DEN) 1-30 days following delivery of litters; other lactating hamsters were given 300, 600 or 1200 mg/kg of dibutylnitrosamine (DBN). Eleven of 15 DEN-treated mothers developed tracheal papillomas and 6 of 15 DEN-treated mothers developed nasal cavity tumors. Among the offspring of DEN-treated hamsters, 12 of 23 developed tracheal papillomas and 1 of 23 developed nasal cavity tumors. Eleven of 15 DBN-treated mothers

developed tracheal papillomas and none of the 15 DBN-treated mothers developed nasal cavity tumors. Among the offspring of DBN-treated hamsters, 5 of 18 developed tracheal papillomas and none of the 18 offspring developed nasal cavity tumors. The latent period for development of tumors in lactating mothers was 8 wk for DEN-treated hamsters and 24 wk for DBN-treated hamsters. The results appeared to suggest that a carcinogenic agent associated with aliphatic nitrosamines could be transmitted from mothers to offspring via milk.

1814 THE ACTIVITY OF GLUCOSE-6-PHOSPHATASE AT DIFFERENT STAGES OF LIVER CANCER DEVELOPMENT: THE EFFECT OF SOME INDUCTORS. (Rus.) Isok, M. E. (Inst. Exp. and Clin. Med., Tallin, U.S.S.R.) and L. E. Teras. *Vop Med Khim* 17(1):40-46, 1971.

The effect of inducing agents such as hydrocortisone, insulin and glucose on glucose-6-phosphatase (G-6-Pase) activity in the liver during diethylnitrosamine (DENA) hepatocarcinogenesis in rabbits and rats was investigated. DENA was given to male rabbits (2.5 mg/kg p.o.) and to white male rats (2.5 or 5 mg/kg for 8 months. Hydrocortisone acetate (5mg/100 g) was given twice daily i.m. for 7 days, insulin (4 U/100 g) s.c. for 2 days and glucose (6.6 ml of a 5% solution) i.p. 6 times within 48 hr at different times during the experimental period. A decrease in G-6-Pase activity (from 1000 to 820 mg P/g tissue) was observed in rabbit liver in the 2nd month of DENA treatment; this activity decreased to 42% during the 5th month and to 30% of the control levels during the 6th, 7th and 8th months of DENA administration. Cessation of carcinogen administration led to a sudden decrease of G-6-Pase to 10% of the normal levels during the 9th month of the experimental period. The rats in the 5 mg/kg DENA-treated group showed a decreased G-6-Pase activity before the occurrence of neoplastic foci; G-6-Pase activity was 50% of control levels at the end of the 8th month of treatment. A 30% decrease of G-6-Pase occurred in the 2.5 mg/kg DENA-treated rats at the end of the 8th month of the experimental period, when hepatomas were macroscopically well defined. Hydrocortisone induced a 40% increase in G-6-Pase activity in both control and DENA-treated animals after 3 months of treatment; it produced no effects starting from the 5th month of treatment although hepatomas occurred only during the 8th month of DENA treatment. The loss of liver cell susceptibility to hydrocortisone was thought to be a pretumorous condition. Minor repression of G-6-Pase (6-10%) induced by insulin was seen in both control and DENA-treated animals during the first 5 months and a slight increase of G-6-Pase occurred after 8 months of carcinogen administration. Glucose had no repressive effects on G-6-Pase during the last period of hepatocarcinogenesis. A loss of liver cell susceptibility towards hormonal alterations was ascertained during the late states of DENA hepatocarcinogenesis.

1815 THE INFLUENCE OF IMMUNOSUPPRESSIVE DRUGS ON CANCERIZATION OF RAT LIVER BY DIETHYLNITROSAMINE AND ON INDUCTION OF FIBROSARCOMA BY 3,4-

BENZPYRENE. (Ger.) Schmähl, D. (German Cancer Res. Ctr., Heidelberg, Germany), R. Wagner and H. R. Scherf. *Arzneimittelforschung* 21(3):403-404, 1971.

Male Sprague-Dawley rats, in whom liver cancerization and fibrosarcoma were chemically induced by diethylnitrosamine (3 mg/kg/day, p.o.) and benzo(a)-pyrene (6 mg/rat, s.c.), resp., were treated at the same time with hydrocortisone (50 mg/kg/wk, p.o.); another group was given cyclophosphamide (13 mg/kg/wk, i.v.) with carcinogen to determine the effects of these immunosuppressors upon tumor production and induction time. A separate group of rats received cyclophosphamide only as control. On the basis of systematic palpation for tumor formation throughout the rats' lifespan no significant effects of these immunosuppressors could be shown on the following parameters: tumor production, induction time, growth rate, and histology of tumors.

1816 THE TRANSPLACENTAL CARCINOGENIC EFFECTS OF N-NITROSODIETHYLAMINE IN MICE. (Rus.)

Likhachev, A. Ya. (N. N. Petrov Res. Inst. Oncol., Leningrad, U.S.S.R.). *Vop Onkol* 17(1):45-50, 1971.

The incidence and morphology of tumors which developed in mice from mothers exposed to diethylnitrosamine (DENA) in mice were investigated. Forty-nine white randbred or C3HA pregnant mice were given DENA (120 mg/kg) 24-48 hr prior to delivery; the offspring were kept with their mothers for 8-10 wk. The incidence of tumors was 76% in the randbred and 82% in the C3HA offspring; spontaneous tumor incidence was 9% in the randbred and 1% in the C3HA controls. The first neoplasm (a squamous cell epithelioma of the esophagus) was noticed in a mouse that died 333 days after transplacental exposure to DENA. Lung tumors were most frequent (31/41 of the randbred and 9/11 of the C3HA mice) and appeared to be papillary, tubular or trabecular adenomas; giant tumors occurred in a few cases and had morphologically detectable malignant foci. Single or multiple tumors developed in 6/41 randbred and 2/11 C3HA mice and appeared to be adenomas of hepatocellular origin sometimes revealing polymorphous structures along with lipid and protein dystrophy. The incidence of leukemia (3/41) in the randbred mice and mammary gland tumors (1/41) was similar in the randbred controls and treated animals; no leukemias occurred in the C3HA offspring. The average latency period was 587 days.

1817 FINE STRUCTURE ALTERATION OF RAT LIVER INDUCED BY NITROSOHEXAMETHYLENAMINE. (E.)

Kim, C. S. (Yonsei U. Coll. Med., Seoul, Korea) and M. Greenblatt. *Yonsei Med J* 11(1):31-41, 1970.

Female rats were given 4 mg of nitrosohexamethylenamine (NHM) in drinking water 5 days per wk for 10 days or 5-22 wk; total doses of NHM ranged from 40-440 mg. Periportal hyperplasia, occasional mitosis and doubly nucleated cells were seen in the liver by light microscopy. In animals exposed to NHM for 10

days and for 5 wk, electron microscopy showed dilated endoplasmic reticulum and Golgi apparatus and an increased number of lysosomes. After 11 wk of NHM feeding, nucleoli of liver cells were enlarged but not segregated and the smooth endoplasmic reticulum showed increased vesiculation. After 14 wk nuclei and nucleoli were markedly enlarged, and after 22 wk there was prominent hyperplasia of the smooth endoplasmic reticulum and increased glycogen particles. Bile canaliculi were dilated and endothelial cells were swollen; an increased number of Kupffer cells were also seen in NHM-fed rats.

1818 GLYCOGEN AND ENDOPLASMIC RETICULUM OF THE LIVER CELL AFTER HIGH DOSES OF THE CARCINOGEN N-NITROSOMORPHOLINE. (Ger.) Theodossiou, A. (Path. Inst. U. Würzburg, Germany), P. Bannasch and W. Reuss. *Virchow Arch Zellpath* 7(2-3):126-146, 1971.

Rats given 50 mg% N-nitrosomorpholine (NNM) in drinking water developed changes in glycogen, endoplasmic reticulum and ribosomes in liver cells, as observed by electron microscopy. All hepatocytes manifested pronounced losses of glycogen, and the endoplasmic reticulum showed loss of organization and proliferation. Some ribosomal reduction and some ribosomal enhancement were seen during maintenance on the carcinogenic regimen. Proliferating endoplasmic reticulum often transformed into an atypical granular condition. Coagulation necrosis was seen in ribosome-deficient cells, while ribosome-rich cells showed high incidences of abnormal mitoses. Ribosomal enhancement, hepatocellular glycogen loss, and increased mitosis reversed within 5 wk after cessation of NNM administration. These changes were not considered to be precancerous, but were changes in response to acute toxic effects.

1819 STUDIES *IN VITRO* ON A POSSIBLE FORMATION OF CANCEROGENIC NITROSAMIDES. (Ger.)

Sander, J. (Hyg. Inst. U. Tübingen, Germany), G. Bürkle, L. Flohe and B. Aeikens. *Arzneimittelforschung* 21(3):411-414, 1971.

The formation of cancerogenic nitrosamides under simulated physiological conditions was investigated as a possible cause of gastric cancer. The formation of nitrosamides from alkylamides at low pH's was determined polarographically. Degradation of methyl and ethyl nitrosourea's occurred in strong acid solutions, the half life being approximately 1 hr at pH 1.0. Methyl and ethyl urethan were nitrosated *in vitro* with progressively higher yields at decreasing pH values, although at these low pH values the nitroso-binding was decreased. Rapidly formed nitroso derivatives were obtained from the incubation of methyl and ethyl urea with nitrite. N-Methylacetamide was not nitrosated to any measurable extent under these conditions. Pilot studies in nitroso derivative formation in animals *in vivo*, have thus far produced negative results in tumor induction.

- 1820 EVIDENCE OF FORMATION OF N-METHYL-N-NITROSOUREA IN RATS GIVEN N-METHYLUREA AND SODIUM NITRITE. (E.) Montesano, R. (Middlesex Hosp Med. Sch., London, England) and P. N. Magee. *Int Cancer* 7(2):249-255, 1971.

Evidence was found for the formation of N(¹⁴C)-methyl-N-nitrosourea in the stomach of rats from nitrosation of N(¹⁴C)-methylurea; the presence of labeled 7-methylguanine was detected in DNA and RNA of several organs of rats administered N(¹⁴C)-methylurea and sodium nitrite. Samples of N(¹⁴C)-methylurea (250 µC, 8.2 mg/ml) were mixed with sodium nitrite solution and administered by stomach tube to rats; 5 hr later the rats were killed and nucleic acids of stomach, liver and small intestine were assayed for incorporation of labeled N(¹⁴C)-methylurea. In rats given N(¹⁴C)-methylurea alone radioactivity was not incorporated into 7-methylguanine of nucleic acids of the stomach tissues. When N(¹⁴C)-methylurea and sodium nitrite were administered simultaneously, incorporation of radioactive label into nucleic acids was much higher than in the N(¹⁴C)-methylurea-treated rats. Ion-exchange chromatograms of hydrolysates of stomach, liver and small intestine nucleic acids showed a radioactive peak corresponding to the altered base 7-methylguanine in rats treated with both N(¹⁴C)-methylurea and sodium nitrite. Apparently the carcinogen N-methyl-N-nitrosourea is formed in the stomach as a result of nitrosation of the corresponding secondary amide.

- 1821 MORPHOLOGICAL STUDIES OF RAT BRAIN TUMORS INDUCED BY N-NITROSOMETHYLUREA. (E.) Schmidek, H.H. (Massachusetts Gen. Hosp., Boston), L. Nielsen, A.L. Schiller and J. Messer. *J Neurosurg* 33(3):335-340, 1971.

Experimental glial tumors induced by injection of N-nitrosomethylurea (5 mg/kg/wk) in Wistar and C.D. Fisher rats were studied for morphological characteristics. Autopsy showed primary brain tumors in 2 of 58 animals surviving the 36 weekly injections, and 11 of these were successfully propagated in both in vivo tissue and tissue cultures and maintained over at least 2 generations. Three low-grade astrocytomas (stable over at least 6 passages), 4 high-grade astrocytomas (stable over 2-14 generations), 2 spindle-cell tumors (stable for 2-4 passages), and mixed gliomas (which evolved into a high-grade astrocytoma and a plasmacytoma and became stable) developed between 17-43 wk after termination of injections. Low-grade astrocytomas revealed indistinct cytoplasmic borders with homogeneous diffuse nuclear chromatin, while high-grade astrocytomas exhibited moderate pleomorphism and stellate areas of necrosis bordered by palisading tumor cells. The predominant pattern in the mixed gliomas was that of numerous elongated, ovoid cells with spindle-shaped nuclei and indistinct cytoplasm and lack of necrosis. Serial subcutaneous transplants provided a stable cell line of low and high-grade astrocytomas for experimental models.

- 1822 BLOOD-BRAIN BARRIER FOR THYMIDINE IN EXPERIMENTALLY PRODUCED TUMORS OF THE CENTRAL NERVOUS SYSTEM OF THE RAT. (Ger.) Citoler, P. (Path. Inst. U. Bonn, Germany), H. J. Drechsler and C. Thomas. *Virchow Arch Zellpath* 7(2-3):260-262, 1971.

Rats in whom tumors of the nervous system had been induced by methylnitrosourea (5 mg/kg/day) were sacrificed 1 hr after i.p. injection of 250 µC of ³H-thymidine, and the intensity of isotope labeling was measured autoradiographically in the cells of the chorioid plexus, gastric mucosa, and of various neurogenic tumors. Cells of the CNS tumors invariably showed clearly lower levels of radioisotope than did those peripheral to the blood-brain barrier including peripheral normal tissues. Some gliomas and all adventitial sarcomas showed areas of many mitoses but without tritium labeling. A varying relative permeability of blood-brain barrier for different tumors is offered as an explanation of these findings.

- 1823 EXPERIMENTALLY INDUCED TUMORS IN GLANDULAR STOMACH IN GUINEA-PIG AND RAT. (Ger.) Bücheler, J. (Path. Inst. U. Freiburg, Germany) and C. Thomas. *Beitr Path* 124(2):194-209, 1971.

Guinea pigs and rats were given methylnitrosourea (MNU) and methylnitrosourea (MNH) in drinking water (2.5 mg/kg) daily. Tumors developed in the stomach and/or pancreas of the guinea pigs and in the rats' glandular stomach after 800 days and 740 days, resp. Of 25 MNH treated guinea pigs developing 12 malignant tumors, 7 tumors were in the region of the stomach and pancreas. MNU produced 26 tumors in 38 guinea pigs, 25 of which were found in the stomach-pancreas region. The types of tumors found were sarcomas (2) and carcinomas (30). Solid, alveolar or scirrhous tumors were found only on the stomach wall; in 3 cases the tumor developed at the site of a chronic gastric ulcer. The pancreas was involved in 5 cases which showed no malignant involvement of the stomach. Glandular stomach tumors developed in 16 rats given acetylmethylnitrosourea (AMNH, in 2 and 4 mg/kg); latency for tumor induction by AMNH was 500 days and 100% of treated rats developed tumors. Two glandular stomach tumors were sarcomas and 16 were adenocarcinomas.

- 1824 ESTABLISHMENT AND SOME CHARACTERISTICS OF NEW TRANSPLANTABLE ASCITES TUMORS PRODUCED BY RAT LIVER CELLS TRANSFORMED IN CULTURE WITH 4-NITROQUINOLINE-1-OXIDE. (E.) Namba, M. (Okayama U. Med. Sch., Japan) and J. Sato. *Gann* 61(6):583-587, 1970.

Rat liver tissue cells were transformed *in vitro* by treatment with 4-nitroquinoline-1-oxide (10⁻⁶M for 20 times over 108 days); the transformed cells produced 2 transplantable lines of ascites tumors when inoculated into rats. The solid tumors were poorly differentiated, and liver cell carcinomas metastasized to lymph nodes and lungs. The tumor lines have been

passaged 30 and 36 times; tumor take occurred in 100% of rats in all generations. The inoculation of 700 cells of one tumor line or 460 cells of the other line killed host animals with 3 months. Tumor cells in both lines lacked glucose-6-phosphatase and glycogen. Sensitivity of one of the tumor cell lines to 4-nitroquinoline-1-oxide was compared with the sensitivity of cells of a hepatoma (AH-66) induced by 4-dimethylaminoazobenzene. The median survival time of rats injected with ascites tumor cells treated with $10^{-4.5}M$ of 4-nitroquinoline-1-oxide was 29 days compared with 21 days for tumor cells not treated with 4-nitroquinoline-1-oxide; animals injected with untreated AH-66 tumor cells survived 12 days compared to 17 days for those injected with cells treated with $10^{-4.5}M$ 4-nitroquinoline-1-oxide. These results indicate that the 4-nitroquinoline-1-oxide-transformed cells did not acquire resistance to the chemical carcinogen.

1825 A PROPOSED MODEL OF THE INTERACTION OF 4-NITROQUINOLINE-1-OXIDE WITH DNA.

(E.) Paul, J. S. (U. Texas Southwestern Med. Sch., Dallas), P. O'B. Montgomery, Jr. and J. B. Louis. *Cancer Res* 31(4):413-419, 1971.

Extended Hückel molecular orbital calculations were made for twenty-seven 4-nitroquinoline-1-oxides (4-NQO) of known carcinogenicity. The following strength of complex formation and presumably the following order of decreasing carcinogenicity were predicted according to the Mulliken population: 6-chloro-4-NQO > 4-NQO > 6-carboxy-4-NQO > 4,6-dinitroquinoline-1-oxide > 4-nitropyridine-1-oxide. Noncarcinogenicity or reduced carcinogenicity was due to the absence of the 4-nitro group or a 1-oxide group or to the presence of bulky substituents in the 2 or 3 position on the quinoline ring. Based upon the experimental evidence and the molecular orbital calculations a possible model of complex formation was formulated hypothesizing a 2-point attachment which involved hydrogen bonding between the oxygen of the 1-oxide group of 4-NQO and the hydrogen of the deoxyguanosine amino group and the transfer of a nonbinding electron from the deoxyribose group to a singly occupied orbital of the nitrogen in the 4-nitro group.

1826 RELATIONSHIP BETWEEN CARCINOGENICITY AND ELECTRONIC STRUCTURE OF MONONITROQUINOLINES.

Kurihara, T. (Lab. Organic Chem., Josai U., Saitama, Japan), H. Ichimura, T. Igaki and A. Ohta. *Chem Pharm Bull* 19(1):37-40, 1971.

The superdelocalizability of 7 mononitroquinoline isomers relative to their carcinogenic properties were investigated by the Hückel method. The carcinogenic isomers, 2- and 4-nitroquinolines, had superdelocalizability values of 1.479 and 1.579, resp., whereas the noncarcinogenic 3-, 5-, 6-, 7-, and 8-nitro isomers had values of 0.173-0.440. These values were considered to be qualitative and it is not clear whether or not a linear relationship exists between carcinogenesis and superdelocalizability values. The reaction indices of several 2- and 4-nitroquinolines with a halogen, methyl or nitro

substituent in the 6-, 8-, and 4- or 2-positions, resp., were given; all had superdelocalizability values greater than 1.00, but biological testing for carcinogenic activity has not yet been done on these compounds.

1827 COMPARATIVE CARCINOGENICITY OF 4-HYDROXY-AMINOQUINOLINE-1-OXIDE AND ITS DIACETYL DERIVATIVES IN MICE AND RATS. (E.) Enomoto, M. (Inst. Med. Sci., U. Tokyo, Japan), E. C. Miller and J. A. Miller. *Proc Soc Exp Biol Med* 136(4):1206-1210, 1971.

Female mice of the CD-1 strain and male rats were treated either topically on shaved dorsal skin or by s.c. injection with 4-hydroxyaminoquinoline-1-oxide (HQ) or its 0,0'-diacetyl derivative (DAHQ). Topical application of 12 μ moles of HQ or DAHQ to mice produced papillomas in up to 50% of mice after latencies of 3-4 months. By 9-12 months after treatment, some squamous cell carcinomas had developed. Both compounds induced sarcomas in 25% of mice given 5 injections of 3.2 μ moles; mice given 10-15 injections of either agent developed sarcomas in 31-57% of cases. Latencies for sarcoma induction in these mice were 4-5 months after the higher number of injections and 6-8 months after the lower number of injections. A single injection of 1 mg of HQ in rats induced fibro- and myosarcomas in 70% of animals within 16 months while equivalent injection of DAHQ induced sarcomas in only 4 of 36 rats given 3 injections. The reason for the comparatively slight carcinogenicity of DAHQ in rats remains obscure.

1828 LATENT MEIOTIC ANOMALIES RELATED TO AN ANCESTRAL EXPOSURE TO A MUTAGENIC AGENT.

(E.) Lavappa, K. S. (Harvard Med. Sch., Boston, Mass.) and G. Yerganian. *Science* 172(3979):171-174, 1971.

Adult male Armenian hamsters were given i.p. injections of ethyl methanesulfonate (100 mg/kg) and bred to normal females. The F_1 generation included 15 males, 2 of which showed chromosomal translocation. These hamsters were bred, and their male offspring were given an i.p. dose of 100 mg/kg urethan; analysis of meiotic bivalents at diakinesis was performed. Urethan produced no chromosomal abnormalities in hamsters grand-sired by untreated animals. However meiotic cells of animals with ethyl methanesulfonate treated grand-sires exhibited 2 distinct forms of cytological abnormalities: association of bivalent end-to-end, leading to a reduction in the number of paired elements in diakinesis; and site-specific deletions of the X chromosome at the junction of positive and negative heteropachytic segments of the long arm. X chromosome deletions and bivalent associations were most frequently observed 6 and 8 days resp., after urethan treatment. Apparently, these anomalies were maintained in a latent state for 2 generations after ethyl methanesulfonate treatment and were made overt by urethan treatment.

- 29 THE ROLE OF REPEATED ADMINISTRATION OF SUCKLING MICE WITH URETHAN ON CARCINOGENESIS. (E.) Matsuyama, M. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan) and H. Suzuki. *Nagoya Med J* (2):105-111, 1970.

7 days of age, mice of strains AKR/JMs and dd/I were given the first of a series of 1-4 s.c. injections of 1 mg/kg of urethan. In AKR/JMs mice, malignant thymic lymphoma developed to a greater extent in mice given multiple doses; by 200 days after birth, 100% of the mice given 4 injections of urethan had died with thymic lymphoma, compared with 60% of the mice given 3 injections, 30% of the mice given 2 injections, 20% of the mice given a single injection, and none of the mice given 4 saline injections (controls). In mice of this strain, spleen, liver, lymph nodes, kidneys and ovaries were also grossly affected. Mice of the dd/I strain, female mice given 2, 3 or 4 injections of urethan developed lymphoma in 75, 83 and 71% of cases, resp., and mice given 1 injection developed lymphoma in 32% of cases. Leukemogenesis was less pronounced in males, but the dose-response observed for females and for AKR/JMs mice was similar. Lung cancer was also seen in dd/I mice; mice given 1 or 3 doses of urethan developed fewer carcinomas than those given 3 or 4 doses. Half the carcinomas induced in dd/I mice were anaplastic.

- 30 A MASSIVE LIPOMA IN A PATIENT RECEIVING CHLORPROPAMIDE THERAPY. (E.) Garfinkel, A. (St. Mary's Hosp., London, England). *Postgrad Med J* 47(544):137-138, 1971.

A 60-yr-old Pakistani male developed a lipoma on his upper back over a period of 16 years which eventually attained dimensions of 30 cm x 24 cm x 20 cm and a weight of more than 5 kg. He had been taking chlorpropamide for a suspected diabetic condition for 16 years. The patient may have had a small lipoma which grew to its final massive size as a result of the chlorpropamide regimen; the tumor may have incorporated glucose into its metabolic pathways more avidly than did the rest of his body due to the increased serum insulin levels brought about by chlorpropamide.

- 31 ADENOCARCINOMA OF THE VAGINA: ASSOCIATION OF MATERNAL STILBESTROL THERAPY WITH TUMOR APPEARANCE IN YOUNG WOMEN. (E.) Herbst, A. L. (Vincent Mem. Hosp., Boston, Mass.), H. Ulfelder and D. Poskanzer. *New Eng J Med* 284(16):878-881, 1971.

Eight cases of carcinoma of the vagina arising in young women 14-22-yr-old were investigated by examining conditions surrounding their births and the births of women of similar ages born in the same hospitals under similar conditions (controls). The lesions included clear cell and endometrial adenocarcinomas. Comparison of patients with matched controls indicated that there was a highly significant correlation between treatment of their mothers with diethylstilbestrol during pregnancy and subsequent development of vaginal carcinoma; 7 of the 8 patients' mothers had taken stilbestrol during preg-

nancy. Maternal bleeding during the pregnancy which produced the carcinoma patient was also correlated with development of carcinoma to a significant degree. Maternal age at time of pregnancy, maternal smoking, intrauterine X-ray exposure, and breast feeding were apparently not related to development of vaginal carcinoma.

- 1832 EFFECTS OF DEPO-MEDROXYPROGESTERONE ACETATE AS A CONTRACEPTIVE AGENT. (E.) Powell, L. C., Jr. (U. Texas Med. Branch, Galveston) and R. J. Seymour. *Amer J Obstet Gynec* 110(1):36-41, 1971.

Of 1,107 women receiving depo-medroxyprogesterone acetate (DMPA) as an oral contraceptive, 23 showed suspicious or positively abnormal cytological cervical smears; this incidence yielded a rate of 21 abnormal cytological smears/1000 patients, which was not thought to be above expectation for the patient group involved -- Negroes of an older age group and high parity. Of 82 patients undergoing histological examination of the cervix, there were 11 cases of dysplasia and 11 instances of carcinoma *in situ*. There were no cases of invasive carcinoma or other genital malignancy. Among children born to women on DMPA after discontinuation of the contraceptive, there was a single instance of hemangioma of the face.

- 1833 THE ROLE OF SMOKING IN THE ETIOLOGY OF LUNG CANCER: EXPERIMENTAL INVESTIGATIONS. (Rus.) Krasnyanskaya, P. N. (Res. Inst. Oncol., Tiflis, U.S.S.R.). *Vop Onkol* 17(1):59-62, 1971.

The effects of smoking Georgian tobacco on the respiratory system in rabbits under conditions comparable to human smoking were investigated. Two experimental groups were used: I) 69 rabbits were exposed to smoking of 9 cigarettes daily (which corresponded to heavy smokers) for 4 yr; IIa) 10 rabbits were given pure benz(a)pyrene (15-20 mg intratracheally single dose) and exposed to smoking 9 cigarettes daily starting 12 days later for 1.5 yr; IIb) 16 rabbits received only benz(a)pyrene as above. Inflammatory processes were seen in group I at the bronchial and bronchiolar level within the first 3 months of the experiment. Irregular hyperplasia of the bronchial and bronchiolar epithelium occurred towards the end of the 1st yr when the animals had smoked 1500-2000 cigarettes. Focal proliferation in the lungs was seen after 1-4 yr when the rabbits had been exposed to 3300-8800 cigarettes. Papillomatous, polypous or adenomatous growth was observed in certain regions of the lung. Combined benz(a)pyrene and smoking exposure (group IIa) induced focal proliferations within 1-1½ yr. Regions of epithelial proliferation could be noticed in the lining of the tracheal epithelium, and no alterations were seen in the nasal epithelium. Cigarette smoking is concluded to be a weak carcinogenic factor for the lung tissue. Group IIa rabbits developed inflammatory changes during the first 3 months; some chronic alterations which developed later were the replacement of normal lung tissue by granular tissue followed by connective tissue.

- 1834 LUNG AND TOBACCO. (Fr.) Fournier, E.
(Hosp. Fernand Vidal, Paris, France) and
P. Zivy. *Poumon Coeur* 26(9):1109-1125, 1970.

The relationship of smoking to various respiratory diseases was studied with particular attention to idiopathic spontaneous pneumothorax. This condition usually appearing after the age of 25 yr, was often linked with smoking and was justified by a statistical analysis which showed a positive correlation between the incidence of this condition and the cigarette consumption of the patient. Among patients with an idiopathic spontaneous pneumothorax condition 36-45-yr-old, 80% smoked more than 15 cigarettes per day while in an age-matched group of healthy subjects, 35% smoked more than 15 cigarettes per day. Various lesions in the lungs were grouped under the diagnosis of "tobacco lung", which is described as a chronic toxic condition with discrete pneumoconiosis, where chronic bronchitis, sclerosis, and bullous emphysema predominated. Smoking apparently provokes the development of the bulla in this condition. Such conditions may lead to fatal consequences either through respiratory insufficiency or through cancerization.

- 1835 LEUKOCYTOSIS DURING LITHIUM TREATMENT. (E.)
Murphy, D. L. (Natl. Inst. Mental Hlth.,
Natl. Inst. Hlth., Bethesda, Md.), F. K. Goodwin and
W. E. Bunney. *Amer J Psychiat* 127(11):1559-1561,
1971.

Circulating leukocyte counts were found to be elevated in 8 manic and 20 depressed psychiatric patients undergoing a course of lithium therapy. Doses of lithium ranged from 1.2-1.8 gm/day, and serum lithium levels in the patients ranged from 0.85-1.30

mEq/l. The increase in venous blood leukocytes in 28 patients averaged 3,600 cells for manic patients and 1,900 cells for depressed patients. Some increase in leukocyte counts was apparent in most patients by the 5th day of lithium administration. During lithium therapy, all 8 of the manic patients but only one of the depressed patients had mean leukocyte counts of over 10,000/mm³; counts exceeded this value in 3 of the manic patients prior to lithium treatments. Leukocyte counts returned to pre-lithium levels within 1 wk after discontinuation of lithium.

- 1836 TOBACCO MOSAIC VIRUS AND POLYPHENOLS AS
NATURALLY OCCURRING CARCINOGENS IN TOBACCO
(Cz.) Chyle, P. (Dept. Med. Microbiol. and Immunol.
KU, Prague, Czechoslovakia), M. Chyle and F. Patock.
Cas Lek Cesk 110(8):188-189, 1971.

- 1837 TOBACCO MOSAIC VIRUS, POLYPHENOLS AND THE
CARCINOGENICITY OF THE TOBACCO HABIT. (Cz.)
Chyle, P. (Dept. Med. Microbiol. and Immunol., KU,
Prague, Czechoslovakia), M. Chyle, J. Korb and M.
Papanek. *Cesk Epidem* 20(1):32-42, 1971.

See also:

- * (Rev): 1740, 1741, 1742, 1743, 1744, 1745, 1747, 1748, 1749, 1750
- * (Viral): 1870, 1896, 1901
- * (Immun): 1982, 1983, 1984, 1985, 1986, 1987, 1988, 1989, 1990, 1991, 1992, 1993, 1994
- * (Path): 2024
- * (Epid-Biom): 2043

PHYSICAL CARCINOGENESIS

38 VIRUS ASSOCIATION WITH ^{90}Sr INDUCED LEUKEMIA OF MINIATURE SWINE. (E.) Frazier, E. (Battelle Mem. Inst., Pacific Northwest Lab., Richland, Wash.), R. N. Ushijima and E. B. Howard. *Bibl Haemat* 36:440-445, 1970.

Preparations from lymph nodes, spleen, kidney, liver and blood plasma of swine in which leukemia was induced by chronic feeding with ^{90}Sr were found to contain virus particles similar in morphology to porcine leukemia virus. In sub-cultures of kidney tissue from leukemic swine, cells appeared to be transformed and harbored C-type viral particles. Primary cell cultures prepared from tissues of leukemic swine showed nuclear inclusions like those found in adenovirus-infected cells in 1-5% of leukemic cells. Swine cells continued to produce infectious adenovirus after 3 months in culture. End-medium harvested from leukemic swine cells produced a cytopathic effect in monolayer cultures of stable porcine embryonic kidney cell line; the agent causing this cytopathic effect was shown to be an adenovirus. The leukemogenic agent in ^{90}Sr -induced swine was thought to be the C-type virus particle, the adenovirus being a contaminant which may or may not enhance the leukemogenic process in these cells.

39 LEUKEMOGENIC EFFECT OF RADIOSTRONTIUM (^{90}Sr) IN MICE: A COMPARATIVE STUDY OF LEUKEMOGENICITY OF ^{90}Sr AND X-RAYS: I. INCIDENCE AND CHARACTERISTICS OF ^{90}Sr -INDUCED AND X-RAY-INDUCED LEUKEMIAS. (Jap.) Ito, T. (Res. Inst. Nucl. Med. Biol., Hiroshima U., Japan). *Acta Haemat Jap* (4):415-431, 1970.

Female mice subjected to 680 r of total-body X-irradiation developed leukemia in 77.3% of cases, after a latency period of 93-208 days; most leukemias were of thymic origin and lymphoblastic cell type. The incidence of leukemia induced by X-irradiation was reduced by thymectomy. Mice given 1 i.p. dose of $1\text{ }\mu\text{C/g}$ ^{90}Sr developed leukemias in 61.8% of cases after latencies ranging from 110-240 days; leukemias induced by ^{90}Sr originated in peripheral lymph nodes but not in the thymus, with the major radiation injury being confined to bone marrow cells. ^{90}Sr -induced leukemias were of lymphoblastic, reticulum cell or stem cell type. Thymectomy of mice did not affect the incidence of leukemias induced by ^{90}Sr . X-irradiation may have produced leukemic progenitor cells in the thymus, bone marrow and/or spleen; progenitor cells may then have migrated to the radiation-injured thymus and proliferated there. ^{90}Sr may have produced similar progenitor cells in the bone marrow by the internal emission of β -rays, with the progenitor cells migrating to peripheral lymphoid tissues. While ^{90}Sr -induced leukemic cells might remain as primitive undifferentiated cells in the peripheral lymphoid cells, X-ray-induced leukemia cells may be able to undergo lymphoid differentiation in the thymus as a result of the action of a hypothetical thymic factor.

1840 LEUKEMOGENIC EFFECT OF RADIOSTRONTIUM (^{90}Sr) IN MICE: A COMPARATIVE STUDY OF LEUKEMOGENICITY OF ^{90}Sr AND X-RAYS: II. TRANSMISSIBILITY OF THE INDUCED LEUKEMIAS, ALKALINE PHOSPHATASE ACTIVITY AND CYTOGENETIC CHANGES OF LEUKEMIC CELLS. (Jap.) Ito, T. (Res. Inst. Nucl. Med. Biol., U. Hiroshima, Japan). *Acta Haemat Jap* 33(4):432-448, 1970.

Newborn mice of various strains were given inoculations of cell-free extract prepared from leukemias induced in mice by i.p. administration of ^{90}Sr or fractionated total-body X-irradiation. Five of 8 cases of leukemia induced by ^{90}Sr were transmitted to recipients with latencies of 73-547 days. The leukemogenic potency of ^{90}Sr -induced cell-free extract was in the 9-33% range. Three of 4 cases of X-irradiation-induced leukemia were transmitted to recipients with latencies of 240-464 days, and the leukemogenic potency of these extracts was comparable to that of extracts of ^{90}Sr -induced leukemias. These results suggested that a virus may play a role in the induction of leukemia by ^{90}Sr and by X-irradiation. In X-ray-induced leukemias, alkaline phosphatase activity was negative or moderate, while in ^{90}Sr -induced leukemias, alkaline phosphatase was markedly elevated. Leukemias induced by ^{90}Sr and transmitted to mice generally showed negative or moderate alkaline phosphatase activity. Aneuploidy, polyploidy and pseudo-polyploidy were common in cells of leukemias induced by ^{90}Sr or X-irradiation. Metacentric, minute and giant chromosomes were seen in 2 leukemias, 1 induced by ^{90}Sr or X-irradiation. Cell-free passaged leukemias originally induced by ^{90}Sr had relatively few chromosome aberrations.

1841 EXPERIMENTAL INDUCTION OF PORCINE LEUKEMIA. (E.) Howard, E. B. (Battelle Mem. Inst., Pacific Northwest Lab., Richland, Wash.). *Bibl Haemat* 36:430-439, 1970.

Pitman-Moore miniature swine which were fed ^{90}Sr in amounts ranging from 1-3100 $\mu\text{C/day}$ developed 69 cases of hematopoietic disease arising, 49 of which were disturbances of myelogenic tissue. There were 29 cases of myeloid metaplasia, 3 cases of stem cell neoplasms, 22 cases of myeloid neoplasms, and 17 cases of lymphoid neoplasms. Myeloid metaplasia was generally associated with higher daily dose levels of ^{90}Sr , as were myeloid neoplasms. In the latter category, pigs showed leukopenia progressing into myeloblastic leukemia at varying times before death. Blast cells in these animals were usually negative for peroxidase and alkaline phosphatase. Granulocytic leukemia, eosinophilic and basophilic leukemia were also observed in the myeloid neoplasm experimental group. Lymphoid conditions, usually lymphoma, generally occurred in the progeny of ^{90}Sr -fed swine. To test the immunocompetence of ^{90}Sr -fed swine, animals were inoculated with *Brucella abortus* antigen and their antibody response was tested by the plate agglutination test. Strontium-fed pigs showed a

reduced capacity to produce antibody to *Brucella* compared to controls, maximum antibody titers in the experimental and control groups measuring 2.5×10^2 and 5.3×10^2 at 1 wk postinoculation.

1842 RADIATION STUDIES ON MICE OF A NATURALLY TUMOR-RESISTANT STRAIN (X/Gf): NUCLEOLAR MORPHOLOGY OF THYMIC LYMPHOCYTES DIFFERING IN RADIO-SENSITIVITY. (E.) Potmesil, M. (Dept. Biol., New York U., New York, N.Y.) and A. Goldfeder. *Radiat Res* 46(2):394-408, 1971.

A tumor-resistant strain of mice (strain X/Gf) was subjected to whole-body X-irradiation in doses of 100-1000 r (single exposure) and were killed 24 hr after irradiation; another experimental group was given a single dose of 300 r and animals were killed 3, 24, 48 or 96 hr or 7 days after irradiation. Thymic lymphocytic cells from irradiated mice were found to have ring-shaped nucleoli, trabeculated nucleoli, dense nucleoli, or nucleoli having combinations of these features. Twenty-four hr after 300 r treatment, the absolute number of mature lymphocytes in mouse thymuses had decreased 80%, the number of promyelocytes by 72%, and the number of lymphoblasts by 58%. Lymphocytes with ring-shaped nucleoli declined more markedly following irradiation than lymphocytes with trabeculated nucleoli, and lymphocytes with both types of nucleoli declined far more markedly than either type. During lymphocyte regeneration, the increase in lymphocytes with trabeculated nucleoli preceded the increase in lymphocytes with the other 2 types of nucleoli. Mature lymphocytes and promyelocytes with ring-shaped nucleoli were found to be the most radiosensitive cell population examined, having a 37% effective dose (D_{37}) of 140 r. Mature lymphocytes and promyelocytes with trabeculated nucleoli had a D_{37} of 335 and 460 r, resp. Lymphoblasts having both ring-shaped and trabeculated nucleoli had a D_{37} of 275 r. Also radioresistant were lymphoblasts with trabeculated nucleoli ($D_{37}=400$ r) and lymphoblasts with dense nucleoli ($D_{37}=500$ r).

1843 FINE STRUCTURE OF ALVEOLAR AREAS IN THE LUNG FOLLOWING INHALATION OF $^{239}\text{PuO}_2$ PARTICLES. (E.) Sanders, C. L. (Batelle-Northwest Lab., Richland, Wash.). R. R. Adey and T. A. Jackson. *Arch Environ Hlth* 22(5):525-533, 1971.

Female rats were exposed to an aerosol of $^{239}\text{PuO}_2$ with an exposure time of 4 min; estimated mean radiation dose in rads absorbed by the lung ranged from 300-13,900 rads. In lung tissue specimens prepared 7 days after exposure to the aerosol, many $^{239}\text{PuO}_2$ particles were seen in macrophages in the lung; the number of macrophages increased in specimens taken from rats exposed at 12, 18-20 and 30 days before preparation of specimens and decreased in specimens prepared 40 and 50 days after exposure. Structural alterations associated with $^{239}\text{PuO}_2$ exposure grew increasingly severe with time after exposure. Plasma cells, histiocytes, septal cells, alveolar exudate, lipid droplets, collagen and elastin all increased from 21 to about 40 days after exposure to

$^{239}\text{PuO}_2$; by 55 days, most changes had either leveled off or decreased. The alveolar exudate was composed of myeloid bodies, cell debris and a protein-like material. During the terminal phase of radiation pneumonitis alveolar type A cells were seen to be damaged.

1844 THE DYNAMICS OF MITOTIC ABERRATIONS INDUCED IN THE WHITE RAT BY A SINGLE DOSE OF 800r. (E.) Anastasiu, Gh. (Med. Fac. Bucarest, Rumania) and O. Cilievici. *Arch Roum Path Exp Microbiol* 29(1-2):81-89, 1970.

In the first 2 days following a single dose of 800 r of X-irradiation, the mitotic index in the femoral bone marrow of rats was at or above control levels (control mitotic index = 10.3%); between 4-15 days postirradiation, mitotic indices dropped to 5.6-8.6% rising again by day 60 to 8.7%. In the first 7 days following irradiation, aberrant mitoses prevailed in rat bone marrow, with more than 50% of mitoses being abnormal. From day 15 forward, however, the percentage of aberrant mitoses declined, and 8% of mitoses were abnormal by day 60 postirradiation. In the first 7 days postirradiation, aberrations including chromosomal fragmentation at the centromere, acentric fragmentation, agglutination, deletion, translocation, gaps and breaks were frequent; from day 15 to day 60, aberrations of the various types began to decrease, and by day 60 only breaks and polyploidies were found. Total aberrations decreased from a high of 201 on day 2 to 18 on day 60.

1845 SPECIFIC PRETUMORAL AND TUMORAL PROCESSES OCCURRING IN MOUSE OVARIES FOLLOWING EXPOSURE TO HIGH DOSES OF IONIZING RADIATION. (Rus.) Aleksandrov, S. N. (Central Res. Inst. Radiol., Leningrad, U.S.S.R.), A. V. Gubareva and K. F. Galkovskaya. *Vop Onkol* 17(1):51-54, 1971.

The dynamics of radiation-induced ovarian tumorigenesis in mice subjected to non-irradiated bone marrow autotransplantation were investigated. Four groups of virgin rambred mice (a total of 600) were exposed to single doses of γ -irradiation of 600, 900, 1100, or 1200 rads, resp., and treated with autologous bone marrow extracted prior to exposure. Three control groups were used: a) intact mice exposed to similar irradiation doses with no further treatment b) non-irradiated mice subjected to bone marrow autotransplant; c) intact mice with no treatment. The animals exposed to 1100 and 1200 rads were given streptomycin (500 U twice daily at 6 hr intervals for 10 days) in addition to bone marrow starting on the 3rd day after the exposure. Bone marrow autotransplant had no effect on the incidence of ovarian tumors in mice exposed to 600 or 900 rads. Whole body irradiation with 1200 rads led to 100% mortality. No hyperplastic alterations of the ovaries were seen during the first months following exposure to 1100 rads in the 203 animals that survived the acute radiation illness stage with the protective autotransplant treatment. Severe vascular damage and long lasting atrophy of the thecal tissue

appeared to be important factors in the development of ovarian tumors. The first tumor, which occurred during the 11th month following exposure to 100 rads, had the structure of a tubular adenoma with an inert stroma; such adenomas are usually rare in animals exposed to lower doses of ionizing radiation. Their average life span was 470 days and similar to that of the animals exposed to 900 rads (477 days), but the tumor incidence of 18% was lower than the latter group and similar to the control groups. Carcinogenesis under conditions of exposure to high doses of ionizing radiation seems to be induced by penetrating radiation effects and to be unrelated to spontaneous blastomogenesis. Decrease of tumor incidence in mice exposed to high doses of irradiation seems to be due to the suppression of gonadotropic activity of the pituitary gland, reflected in the atrophy of the ovarian theca, and to severe vascular damage.

- 46 THE POSSIBLE CARCINOGENIC EFFECTS OF RADIATIONS ON THE UTERUS. (E.) Bird, C. (Imp. Cancer Res. Fund, London, England) and A. Willis. *Brit J Cancer* 24(4):759-768, 1970.

The carcinogenic effects of radium and X-rays on the rat uterus were studied with the object of determining successful induction of mixed endometrial tumors in response to radiation. In 20 rats treated with radium, 2 developed adenocarcinoma and a squamous cell carcinoma by comparison to 10 control rats with negative findings. Of 10 rats treated with 500 rad X-rays, 1 developed a leiomyoma; with 1000 rad, 1 adenocarcinoma and 1 adenosarcoma were found among 10 rats. Nineteen allografts treated with 500 rad and 1000 rad resp., failed to develop tumors; endometrial polyps occurred in a proportion of the rats in all groups receiving radium X-ray treatments. A variety of other extrauterine tumors occurred in both irradiated and control rats with mean tumor induction significantly reduced to 44.6 and 50.0 wk with 500 and 1000 rad dose, resp., compared to 73.6 wk in controls. Mammary tumors, principally adenocarcinomas and fibroadenomas, were found most frequently in the allografted X-irradiated rats. Experiments show that endometrial adenocarcinomas can be induced by intrauterine radium application or X-irradiation of the uterus from without.

- 47 INDUCTION OF MAMMARY NEOPLASIA AFTER IN VITRO EXPOSURE TO X-RAYS. (E.) Hellabarger, C. J. (Brookhaven Natl. Lab., Upton, N.Y.). *Proc Soc Exp Biol Med* 136(4):1103-1106, 1971.

Dominal-inguinal mammary tissue was excised from rats and exposed to a total of 800 r X-irradiation over a 2 min period; irradiated and sham-irradiated tissues were then replaced in the rats from which they had been taken. Of 110 irradiated grafts, 16 had developed mammary neoplasia 10 months after the graft; of the 16 neoplasms, 13 were fibroadenomas and 3 were adenocarcinomas. Of the 110 sham-irradiated

mammary tissue grafts, 1 developed neoplasia (a fibroadenoma). *In situ* neoplasia was found in 8 of the 110 rats given irradiated grafts; 6 of these neoplasms were fibroadenomas, 2 on the side opposite the side receiving the mammary tissue graft.

- 1848 THE ROLE OF MICROENVIRONMENTAL FACTORS IN HEMATOLOGIC RESPONSE OF MICE EXPOSED TO 1000 R "SPLIT DOSE" IRRADIATION AND TESTOSTERONE TREATMENT. (E.) Hajdukovic, S. (Biol. Div., Inst. "Boris Kidric", Belgrade, Yugoslavia). *Strahlentherapie* 141(4):464-471, 1971.

C57BL mice were exposed to 400 r of whole body irradiation followed by a dose of 600 r administered to the exteriorized spleen and hind leg. Following irradiation, the mice were treated with 2.5 mg of testosterone. During the first wk after irradiation, testosterone treated mice showed decreases in spleen weight. During the second postirradiation wk, spleen weight increased markedly in groups receiving testosterone treatment immediately after irradiation. Increases to a lesser degree were found in mice receiving testosterone treatment which had been delayed 24 hr or more after irradiation. The number of spleen cells was very depressed 8-10 days after irradiation in all testosterone treated mice. This contrasted with an increased spleen cell count found in the control group. During the second postirradiation wk the number of spleen cells increased in mice receiving testosterone immediately after irradiation. No similar increase was found in mice receiving delayed testosterone treatment. Testosterone treatment, whether initiated immediately after irradiation or later, stimulated erythroid regeneration in the bone marrow. Irradiated mice not treated with testosterone did not show stimulation of erythroid regeneration.

- 1849 RADIATION-INDUCED FIBROSARCOMA. (E.) N. F. C. Gane (Mount Vernon Hosp., Northwood, Middlesex, England), R. Lindup, P. Strickland and M. H. Bennett. *Brit J Cancer* 24(4):705-711, 1970.

In a series of 220 patients with fibrosarcoma, 6 cases were discovered in which the development of the lesion followed massive doses of therapeutic X-irradiation. Patients developed fibrosarcomas at the orbit, tongue, chest wall and femur after periods of 5-33 yr had elapsed since doses of X-irradiation ranging from 2600-8000 r had been administered.

- 1850 INTERFERENCE-MICROSCOPIC STUDY OF DRY WEIGHT AND WATER CONTENT IN BRONCHIAL EPITHELIAL CELLS IN RABBITS AFTER Co^{60} -GAMMA IRRADIATION. (Ger.) Nikulin, A. (Med. Fac. Sarajevo, Yugoslavia), B. Pikula, P. Plamenac and J. Djordjevic. *Beitr Path* 142(3):235-243, 1971.

Rabbits were exposed to Co^{60} γ -irradiation (4,760 r), and cells from their bronchial epithelium were removed and studied by interference microscopy. The volume and water content of bronchial epithelial cells'

nuclei and cytoplasm were increased by 60% and 23%, resp., in the first 12 hr postirradiation. Fluid contents of nuclei and cytoplasm declined after 3-4 days postirradiation, but did not approach normal levels until 10 days postirradiation. The dry weight of nuclei and cytoplasm increased following irradiation, but the dry weight increase was not as marked as the increase in water content. Osmotic changes brought about by irradiation were thought to have caused the changes in volume and water content of irradiated cells.

- 1851 *IN VITRO* IRRADIATION OF EMBRYONIC HAMSTER FIBROBLASTS WITH ULTRAVIOLET LIGHT OF 280 nm. (Ger.) Buder, E. (German Acad. Sci., Berlin, Germany), I. Rahn, T. Schramm and R. Wetzell. *Arch Geschwulstforsch* 36(4):335-338, 1970.

Fibroblast cultures from embryonic golden hamster tissues cultivated for 21-40 days were irradiated 5-10 times with UV light at 280 nm at a previously empirically determined optimal dosage of 1.0×10^4 erg/cm². The 40-day cultures were harvested manually and 1×10^6 to 5×10^6 cells, suspended in nutrient medium, were injected s.c. in each of a series of 48 hr old Syrian hamsters. Systematic examination over 5-7 months failed to disclose any evidence of tumor formation in the 21 animals treated. Similarly, *in vitro* preparations showed no indications of malignant cell forms. The findings in these experiments using 280 nm light are considered negative.

- 1852 EPITHELIAL OUTGROWTHS FROM LUNG TISSUE FOLLOWING INTRAPLEURAL INJECTION OF ASBESTOS DUST IN EXPERIMENTAL ANIMALS. (E.) Davis, J. M. G. (Dept. Path., Cambridge U., England). *Int J Cancer* 7(2):238-248, 1971

Chrysolite and crocidolite asbestos dust particles (25 mg suspended in water) were injected into the pleural cavity of rats, mice and hamsters, and the animals were examined for pleural lesions at intervals from 7 days to 4 yr later. Treated animals developed granulomas and areas of the pleural surface became thickened with fibrous tissue. Granuloma cells either phagocitized or surrounded the injected dust. Clefts lined with epithelial cells formed outside the original line of the pleural surface and grew into the granulomas and areas of fibrous pleural thickening. The cells in these clefts, while originally showing the structure of surfactin-secreting alveolar cells, later lost their surfactin granules and became ciliated. Cysts formed from clefts in some animals, and groups of cysts grew from the lung tissue to invade the areas of pleural fibrosis. Like the clefts, the cysts were lined with surfactin-secreting alveolar cells.

- 1853 CARCINOGENIC PROPERTIES OF WEAR PARTICLES FROM PROSTHESES MADE IN COBALT-CHROMIUM ALLOY. (E.) Heath, J. C. (Strangeways Res. Lab., Cambridge, England), M. A. R. Freeman and S. A. V. Swanson. *Lancet* 1(7699):564-566, 1971.

Prosthetic devices for the replacement of hip and knee joints were worked mechanically in a medium containing either Ringer's solution or synovial fluid at 37°C, and a deposit of wear particles was collected. The prostheses were made of a cobalt-chromium alloy, and the wear particle deposits consisted of 66% cobalt and 26% chromium. Samples of the wear debris were injected into skeletal muscles of female rats. Fourteen rats developed sarcomas 4-15 months after injection of the debris. Tumors included osteofibrosarcomas, cellular sarcomas and anaplastic rhabdomyofibrosarcomas. Tumors metastasized to lymph nodes in the thigh and to the prevertebral lumbar region.

- 1854 MEDICAL X-RAY EXPOSURE AMONG HIROSHIMA AND NAGASAKI A-BOMB SURVIVORS. (E.)

Russell, W. J. (Atomic Bomb Casualty Comm., Hiroshima Japan). *Nippon Acta Radiol* 30(10):12-54, 1971.

Of 20,000 persons examined in Hiroshima and Nagasaki since 1957, 23% of the Hiroshima and 12% of the Nagasaki group had received therapeutic or diagnostic X-irradiation. More survivors of the nuclear bomb attacks on Hiroshima and Nagasaki reported exposure to medical X-rays than did persons not exposed to radiation at the time of the attacks in 1945. In Hiroshima, the sites most frequently exposed to therapeutic X-irradiation were the lymph nodes of the neck, the thyroid and the uterus. Cumulative medical X-ray doses approached doses incurred by atomic bomb survivors who were 2200 m from the explosion hypocenter in Hiroshima and 3200 meters from the hypocenter in Nagasaki. Skin doses of X-irradiation averaged 43.5 rads in Hiroshima and 12.8 rads in Nagasaki. Gonadal doses in Hiroshima and Nagasaki for males were 118 and 37.4 mrad, resp, and for females, 1652 and 413 mrad, resp. The integral bone marrow dose in Hiroshima and Nagasaki was 1269 and 454 g-rads, resp.

- 1855 ULTRASTRUCTURE OF HUMAN EPIDERMIS FOLLOWING CHRONIC SUN EXPOSURE. (E.) Everett, M. A. (U. Oklahoma Med. Ctr., Oklahoma City), J. Nordquist and R. L. Olson. *Brit J Derm* 84(3):248-257, 1970.

Biopsy specimens from 6 elderly, fair-skinned male farmers were prepared from areas of the body exposed to sunlight and from unexposed areas; the patients had histories of actinic keratoses and skin cancer. Under the light microscope, the exposed skin showed effaced rete ridges and decrease in epidermal thickness. Ultrastructurally, unexposed skin showed no prominent abnormalities; exposed skin showed great variability in quantity and morphology of desmosomes, ribosomes, endoplasmic reticulum, mitochondria and melanosomes. Keratinocyte morphology varied from normal to severely disordered. Abnormal tonofilament morphology within basal cells was the most consistent and characteristic abnormality; most tonofilaments were abnormally short, and filaments were often fused. Degenerative changes resembling dyskeratosis were seen in spinous and basal cells, and cellular cohesion was

disturbed. Melanin distribution in exposed skin was abnormal, varying from areas of excessive melanin content to areas in which pigment was absent. Melanosome complexes were often larger than normal. These changes in exposed skin were often seen under the electron microscope when no light microscopic or clinical abnormalities were observable.

1856 EFFECTS OF LIGHT ON SKIN LIPID METABOLISM.
(E.) Black, H. S. (VA Hosp., Houston, Tex.) and E. W. Rauschkolb. *J Invest Derm* 56(5): 387-391, 1971.

Fresh human skin obtained from the lower abdomen of male Caucasian subjects was exposed to broad-spectrum light in doses which exceeded by a factor of 10 the amount of light needed to produce erythema. Six hr after exposure, total lipid, free sterol, neutral fat and phospholipid were assayed in the irradiated skin. Values for total lipid incorporation of C^{14} -acetate were 51% of control values in irradiated skin, and phospholipids in irradiated skin were at 15% of control values. Sterols in irradiated skin incorporated 48% of the C^{14} -acetate incorporated by control sterols, and neutral fat incorporation was 47% of the value of control fat incorporation in irradiated skin. Levels of C^{14} -acetate incorporation into digitonide-precipitable sterols in irradiated skin were 58% of their values in controls, while levels of C^{14} -mevalonate incorporation into these sterols in irradiated skin were 96% of control values. Studies on porcine skin suggested that the reduction in acetate incorporation into lipids resulted from altered synthesis of lipids. The light susceptible site of sterol synthesis was thought to lie along the biosynthetic pathway between acetate and mevalonate.

1857 STUDY OF ASBESTOS WORKERS IN BRITISH COLUMBIA. (E.) Hurlburt, J. F. (Dept. Med. III, U. British Columbia, Vancouver, Canada) and N. G. Schulson. *Brit Columbia Med J* 13(3):58, 67-68, 1971.

Thirty-three asbestos workers from the Vancouver area, 20 with histories of exposure in excess of 20 yr, were tested to determine whether exposure to asbestos dust had impaired pulmonary function. Twelve of the 33 men tested had chronic coughs; 22% of the former cigarette smokers and 70% of all present cigarette smokers had chronic coughs. Three men who had been exposed to asbestos dust for more than 10 yr had experienced recurring asthmatic attacks. Six of the 33 men tested had vital capacities that were below 80% of the predicted normal values in pulmonary function tests; all these men had been exposed to asbestos dust for more than 15 yr. Thirteen of the subjects showed abnormally low (i.e., below 75% of normal) forced expiratory volume in 1 second. Abnormal scores in forced expiratory volume tests among asbestos workers were found to be correlated with cigarette smoking; 70% of all those with abnormal scores were present smokers. Cytological screening showed 1 subject with Class II and another with possible Class II cells. One sub-

ject showed scattered opacities in the upper portions of the right lung which may have represented pleural plaques.

1858 DIFFUSE MALIGNANT PLEURAL MESOTHELIOMA AND ASBESTOS EXPOSURE. (E.) Whitwell, F. (Broadgreen Hosp., Liverpool, England) and R. M. Rawcliffe. *Thorax* 26(1):6-22, 1971.

Of 52 cases of pleural mesothelioma collected in the Liverpool area from 1955-1970, 20 were cases of tubulo-papillary tumor and 11 were sarcomatous, with 18 cases of "mixed" histological type. The tumors were invasive and metastasizing; distant metastases were found in 14 of 22 necropsies among the 52 cases. Common sites for blood-borne metastases were the liver and lung. Seventy-five percent of the patients were between 50-70-yr-old, and 77% of them were male. Fifty-three percent of the patients survived 1 yr from the onset of pleural mesothelioma symptoms, 17% survived 3 yr and 8% survived over 5 yr. Thirty-five of 40 male cases and 8 of 12 female patients had experienced significant exposure to asbestos dust in the course of their working lives, often as employees in the shipbuilding industry in Liverpool. Duration of exposure to asbestos dust ranged from 3 to more than 50 yr, and the interval between first asbestos exposure and onset of mesothelioma symptoms usually exceeded 25 yr (mean = 42 yr). Seventeen percent of the patients showed basal asbestosis in their lungs, and asbestos bodies were found to excess in the lungs of nearly all the patients.

1859 HISTOLOGIC TYPES OF LUNG CANCER AMONG URANIUM MINERS. (E.) Saccomanno, G. (VA Hosp., Grand Junction, Colo.), V. E. Archer, O. Auerbach, M. Kuschner, R. P. Saunders and M. G. Klein. *Cancer* 27(3):515-523, 1971.

In a survey of 121 cases of lung cancer among American uranium miners, the frequency of incidence of oat cell carcinoma and small cell undifferentiated (polygonal cell) carcinomas was found to increase with radiation exposure up to 1500 working level months (WLM). At 1500 WLM, 50% of the cancers observed were small cell undifferentiated polygonal cell type and 25% were small cell undifferentiated oat cell type. Epidermoid carcinomas and other types of carcinoma decreased in incidence to 2000 WLM of exposure, with frequencies leveling off at higher exposures; 17% of cancers were epidermoid cancer and 5% were other carcinoma cell types at 3000 WLM. An average of 15.9 yr was round to elapse between beginning of mining and onset of cancer. Workers exposed to uranium radiation for 2501-9700 WLM showed the longest induction-latent period (18.2 yr) and workers exposed to radiation for 201-700 WLM showed the shortest induction-latent period (10.6 yr). In miners of all ages and with all observed histories of cigarette smoking, exposure to radiation increased the incidence of small cell undifferentiated carcinoma and decreased the incidence of epidermoid carcinoma. Although the frequency of epidermoid cancer was greater among older miners than among younger miners, there was no observable correlation between epidermoid carcinoma

and cigarette smoking. Younger heavier smokers had higher frequencies of oat cell carcinoma than light smokers of the same age.

- 1860 GENERALIZED PARAFFINOMA (SCLEROSING LIPO-GRANULOMA). (E.) Urbach, F. (Temple U. Hlth. Sci. Ctr., Philadelphia, Pa.), S. S. Wine, W. C. Johnson and R. E. Davies. *Arch Derm* 103(3): 277-285, 1971.

Sclerosing lipogranuloma was developed by a 30-yr-old woman who had received multiple injections of mineral oil totaling 1 liter in the calves of her legs. Less than 2 yr after the treatment, large plaques of indurated thickened skin appeared on her legs. Roentgenograms of the chest showed fine nodular densities scattered throughout both lungs; these were thought to be secondary to microembolization of lipid from the mineral oil injections in the legs. Pulmonary function tests showed an inspiratory capacity 50% of the predicted norm. Sclerosing lipogranuloma was found in skin from the right calf and thigh. Sections from the lung showed many noncaseating granulomatous lesions with large multinucleated giant cells. Sections of lymph node showed many tissue spaces. Mineral oil was determined to be the agent responsible for the changes observed in the patient's tissues.

- 1861 ADENOCARCINOMA ARISING IN A GIANT RENAL CYST: REPORT OF A CASE. (Jap.) Kato, T. (Fac. Med. Kyoto U., Japan) and Y. Fujimoto. *Acta Urol Jap* 16(12):728-730, 1970.

- 1862 THOROTRAST-INDUCED LATE DAMAGE OF THE RETROMANDIBULAR REGION AFTER ANGIOGRAPHY OF THE CAROTID. (Ger.) Manzke, E. (Katherine Hosp. Stuttgart, Germany). *Z Laryng Rhinol Otol* 50(1):33-40, 1971.

- 1863 OSTEOGENIC SARCOMAS IN MICE AFTER TRAUMA OF THE EXTREMITY AND WHOLE BODY IRRADIATION. (Rus.) Gubareva, A. V. (Central Sci. Res. Inst. Roentgen and Radiol. Leningrad, U.S.S.R.), S. N. Aleksandrov, K. F. Galkovskaya and K. B. Shimanovskaya. *Vop Onkol* 16(12):23-26, 1970.

- 1864 THE ROLE OF DIRECT AND INDIRECT IONIZING RADIATION IN LEUKEMOGENESIS. (Rus.) Aleksandrov, S. N. (Central Res. Inst. Roentgen and Radiol., Leningrad, U.S.S.R.), K. F. Galkovskaya and A. V. Gubareva. *Vop Onkol* 16(11):80-85, 1970.

See also:

- * (Rev): 1742
- * (Chem): 1804
- * (Viral): 1868, 1870
- * (Epid-Biom): 2046

VIRAL CARCINOGENESIS

365 LEUKEMIA OF GUINEA PIGS. (E.) Ioachim, L. (Lenox Hill Hosp., New York, N. Y.) and L. Warwick. *Bibl Haemat* 36:566-573, 1970.

Transmission of a spontaneous leukemia arising in guinea pigs by inoculation of animals with suspensions of leukemic cells or with plasma produced leukemias in recipient guinea pigs within 12-15 days after injection of cell suspensions and after 18-20 days following injection of plasma. In inoculated guinea pigs, white blood cell counts rise from 2-100,000 elements/ml. Leukemic guinea pigs died within a few days after onset of symptoms, and the major organs involved were spleen, liver and lymph nodes. Virus particles having diameters of 800-1000 Å were found in leukemic guinea pigs in the area of the nuclear envelope and in the cisternae of the endoplasmic reticulum of cells. These particles had the shape of C-type particles, but their nucleoids were not as electron-dense as those of C-type particles. Leukemia could not be induced by inoculating guinea pigs with cell-free filtrates of leukemic cells.

366 COMPARISON OF LEUKEMOGENIC AND SARCOMAGENIC VIRUSES AT THE ULTRASTRUCTURAL LEVEL. (E.) Ochowski, L. (U. Texas M.D. Anderson Hosp. Tumor Inst., Houston). *Bibl Haemat* 36:62-82, 1970.

Following a review of the literature of the morphology and species-specificity of RNA viruses, a comparison of leukemogenic and sarcomagenic RNA virus particles in animals of different species at the ultrastructural level was described. Mouse mammary tumors harbored virus particles not easily classified as either B or C type; particles took several different forms including budding forms, multinucleate forms and amorphous forms. Particles found in murine leukemias, solid tumors and in some mammary tumors included mature and immature forms. B and C type virus particles were found in some mouse mammary tumors, as were particles of an undefined type resembling "H" type particles. Murine leukemias and reticulum cell sarcomas contained characteristic cylindrical particles. Type "H" particles were found in rat and hamster bone tumors as well as in mammary tumors. Type C particles differing in the density of the nucleoid of particles in different tumors were found in bone tumors of mice, in feline lymphomas, and in human leukemias. Esh sarcomas also contained type particles like those found in chickens with Marek's disease.

367 STUDIES ON THE CONJECTURAL VIRUS NATURE OF HUMAN LEUKEMIA IN EXPERIMENTS ON MONKEYS. (E.) Yakovleva, L. A. (USSR Acad. Med. Sci., Sukhumi). *Bibl Haemat* 36:761-772, 1970.

Macaque monkeys (*Macaca mulatta* and *M. speciosa*) and hamadryas baboons (*Papio hamadryas*) were inoculated with whole heparinized or citrated blood from human patients with stem cell leukemia or chronic myeloid leukemia. Inoculated monkeys included newborns of both sexes, fetal monkeys, pregnant females and adults of both sexes aged from 1-3 yr. Inoculations

produced enlarged lymph nodes and splenomegaly in macaques, often leading to death; autopsy revealed focal proliferation of young reticular and undifferentiated blast cells in bone marrow and spleen. *M. speciosa* were more susceptible to the effects of the inocula than were *M. mulatta*. Baboons did not develop the symptoms observed in macaques; however, some inoculated female baboons developed symptoms of leukosis-reticulosis by 1.5 yr postinoculation. Among both macaques and baboons, pregnant females inoculated with leukemic cells *in utero* during pregnancy were especially susceptible. Uninoculated monkeys maintained in the vicinity of the inoculated animals developed mild leukemias. Leukocytes of all affected monkeys were found to possess a surface antigen. The passage of blood from inoculated and symptomatic monkeys to other monkeys produced symptoms similar to those manifested by the donors, and recipient animals demonstrated the surface antigen found in affected inoculated monkeys.

1868 SIGNIFICANCE OF VIRUS PARTICLES OBSERVED IN SPONTANEOUS AND INDUCED TUMORS OF THE SYRIAN HAMSTER. (E.) Stenback, W. A. (Baylor Coll. Med., Houston, Tex.), G. L. Van Hoosier, Jr., D. B. Ferguson and J. J. Trentin. *Bibl Haemat* 36:559-565, 1970.

An isolated and supposedly virus-free hamster colony was surveyed for tumor incidence and for the presence of viruses. Of 106 hamsters tested for viral antibodies by means of the hemagglutination inhibition test, 2 were found to harbor antibodies to reovirus type 3. Of 1671 animals in the colony, 8 developed spontaneous malignant neoplasms which were detected at necropsy at 188 days of age or older. Six of these tumors arose in hamsters 12 months of age or older, and 3 of them were lymphomas involving lymph nodes. Other tumors were kidney carcinoma, adenocarcinoma metastasizing to the mesenteric lymph nodes, myxoid liposarcoma of the cheek pouch, hemangio-pericytoma of the cheek pouch and undifferentiated sarcoma involving the subcutis. C-type particles were found in lymphomas, and "Bernhard" virus particles were also found to be endemic in hamsters in the colony. One malignant lymphoma arose in 1 of 29 hamsters exposed to 4 equal doses of 240 r irradiation at 7 day intervals; this tumor was transplantable and contained clusters of A-type viral particles, as well as C-type and "Bernhard" virus particles.

1869 INTRACISTERNAL TYPE A PARTICLES AND PROPERTIES OF A CONTINUOUS CELL LINE ORIGINATING FROM A GERBIL FIBROMA. (E.) Tumilowicz, J. J. (Inst. Med. Res., Camden, N. J.) and J. J. Cholon. *Proc Soc Exp Biol Med* 136(4):1107-1110, 1971.

An explanted fibroma from the dorsal surface of the paw of a gerbil was prepared for culture and passaged more than 70 times. The tumor consisted of fibroblast-like cells and had a doubling time in culture of 36-38 hr. In the fifth passage, the modal chromosomal number of the tumor cells was 44 with 22% of the cells deviating from this norm; by passage 52,

all cells examined were heteroploid. Ultrastructurally, the salient features of the gerbil fibroma cell line were well developed rough endoplasmic reticulum often showing distended cisternae, intricately ruffled or lobed nuclear membranes, and a particle resembling the intracisternal A-type particle. Type A particles were rare and were usually solitary; budding particles were extremely rare. Although particles were found in cells in culture, none could be found in cells from the tumor itself. No mycoplasma could be isolated from the tumor cells. The cells were susceptible to adenovirus 12, herpes simplex virus and reovirus 3, and resistant to poliovirus 1 and echovirus 11. Hamsters inoculated with gerbil fibroma cells developed regressing nodules but no progressive tumors.

- 1870 'C'-TYPE VIRUS PARTICLES IN RAT TUMORS. (E.) Chopra, H. C. (John L. Smith Mem. Cancer Res., Chas. Pfizer & Co., Maywood, N. J.) and R. M. Dutcher. *Bibl Haemat* 36:584-592, 1970.

Mammary carcinomas induced in rats by various means and transplanted rat leukemias were examined microscopically for the presence of C-type virus particles. Rat mammary tumors were primary and/or transplantable dimethylbenzanthracene-induced carcinomas, tumors induced by methylcholanthrene, diethylstilbestrol-cholesterol-induced tumors, spontaneous tumors, X-ray-induced tumors and mammary adenocarcinoma R-35. Virus-like particles resembling C-type particles were found in neoplastic cells of transplanted mammary tumors but not in primary tumors; C-type particles were most abundant in mammary adenocarcinoma R-35. Older necrotic tumors and new transplants yielded the least amounts of particles. C-type particles were scarce in transplanted methylcholanthrene- and diethylstilbestrol-cholesterol-induced tumors. Rat leukemias also contained C-type particles; however, the size and morphology of these particles was more variable than those seen in mammary tumors.

- 1871 L₂C/NB GUINEA PIG LEUKEMIA: FAILURE TO DEMONSTRATE TRANSMISSIBLE LEUKEMOGENIC VIRUS. (E.) Sarma, P. S. (Natl. Inst. Hlth., Bethesda, Md.), P. J. Ueberhorst, V. Zeve, J. Whang-Peng and R. Huebner. *Bibl Haemat* 36:574-577, 1970.

Although it was not possible to transmit leukemias from L₂C strain 2 guinea pigs by means of cell-free filtrate inocula, the leukemia could be transplanted by inoculation of viable leukemic blast cells i.p., s.c., or intradermally to recipient guinea pigs. As few as 12 leukemic blast cells in the inocula successfully transmitted the disease. *In vitro* attempts to isolate and demonstrate a C-type RNA virus in leukemic guinea pig cells gave negative results; no antigens similar to avian or murine leukemia group-specific complement fixing antigens could be detected in guinea pig leukemic cells by complement fixation tests. Virus particles were not seen in guinea pig embryo fibroblast cultures inoculated with cell-free preparations of strain 2 guinea pig leukemic tissue. Chromosomal studies appeared to indicate that the fatal leukemia seen in strain 2 guinea pigs was caused by the proliferation of blast cells transplanted from the original leukemia which was from a strain 2 female guinea pig.

- 1872 BIOLOGICAL STUDIES WITH VIRAL INDUCED FIBROSARCOMAS IN CATS, DOGS, RABBITS AND NON-HUMAN PRIMATES. (E.) Theilen, G. H. (U. California Sch. Vetr. Med., Davis), S. P. Snyder, L. G. Wolfe and J. C. Landon. *Bibl Haemat* 36:393-400, 1970.

Fibrosarcomas induced in cats by virus and spontaneous fibrosarcomas served as the source for inocula which were given to kittens, puppies, rabbits, marmosets and monkeys of the genus *Macaca*. Fibrosarcomas were induced in all recipient groups with varying incidences. Of 65 kittens inoculated with filtrates or extracts from feline fibrosarcoma, 39 developed s.c. fibrosarcomas with a latency of 10-45 days; tumors were multiple and most were progressive. Fibrosarcoma filtrate developed tumors with latencies of 8-28 days; tumors were similar to those developed by kittens. All 3 rabbits given fibrosarcoma filtrates developed multiple tumors at the site of inoculation; the latent period was 12-20 days. No viral particles were found in the fibrosarcoma cells. Two marmosets given i.p. and s.c. inoculations of fibrosarcoma extracts developed invasive inguinal and intra-abdominal tumors after a latent period of 24-28 days; no C-type virions were seen in the neoplastic cells. *Macaca* monkeys developed tumors in 5 of 6 cases 15-17 days after inoculation. No viral particles were observed.

- 1873 FURTHER CHARACTERIZATION OF BOVINE LEUKEMIC CELL CULTURES. (E.) Lin, P. S. (Sch. Vetr. Med., U. Pennsylvania, Kennett Square), G. B. Guest, N. D. Stock and R. M. Dutcher. *Bibl Haemat* 36:465-470, 1970.

Indirect immunofluorescence tests carried out with bovine sera against infectious bovine rhinotracheitis virus and anti-parainfluenza III virus failed to show reactions with suspensions of cell lines established *in vitro* from mononuclear leukocytes of cattle with lymphosarcoma. However, all the bovine lymphosarcoma cell lines tested did react directly with bovine syncytial virus (BSV) fluorescein conjugated serum. The possibility that the lymphosarcoma cell lines contained BSV was further supported by the finding that syncytia appeared in subcultures of bovine lymphosarcoma cells co-cultivated with bovine embryonic monolayer cultures. Assays of supernatant fluids from lymphosarcoma cell lines were negative for interferon, and electron microscopic examination of lymphosarcomatous cell lines revealed no virus-like particles. Calves injected with cells from mixed cultures did not develop lymphosarcoma or leukemia; however, the lymphocyte counts of inoculated calves were above expectation.

- 1874 COMPARISONS OF VIRUS-LIKE PARTICLES FROM LEUKOTIC CATTLE TO FELINE LEUKOSIS VIRUS. (E.) Kawakami, T. G. (Sch. Vetr. Med., U. California Davis), A. L. Moore, G. H. Theilen and R. J. Munn. *Bibl Haemat* 36:471-475, 1970.

Virus-like particles purified from plasma of leukotic cattle had a buoyant density comparable to that of

feline leukemia virus; the bovine virus rested in sucrose gradients between 1.14 and 1.18 g/cm³. The sedimentation rate of the bovine virus-like particles was less than that of the feline leukemia virus, and the bovine particles were more variable morphologically than feline leukemia virus. Bovine virus-like particles were about 85-100 nm in diameter, whereas the diameter of the feline leukemia virus is approximately 115 nm. Bovine virus-like particles, like feline leukemia virus, appeared to replicate from lymphocytes by budding. No antigenic interactions between bovine virus-like particles and feline leukemia virus could be demonstrated by immunodiffusion tests.

- 1875 FURTHER STUDIES OF BOVINE SYNCYTIAL VIRUS. (E.) Van Der Maaten, M. J. (Agric. Res. Service, Ames, Iowa), A. D. Boothe and W. A. Almquist. *Bibl Haemat* 36:446-452, 1970.

Immunodiffusion tests were run on sera from 9 species to determine the presence in these species of bovine syncytial virus antigen; species tested were: mouse, hamster, guinea pig, rabbit, sheep, swine, bison, horse and man. None of the sera reacted positively. Five 10 of 10 rabbits and 2 of 4 sheep inoculated with bovine syncytial virus became infected with virus, no infection was produced by inoculation of mice, hamsters, guinea pigs or swine. Rabbits were infected successfully whether given concentrated or dilute virus inocula. Virus particles were found at surface membranes of cells of infected bovine embryonic spleen cells. Additional instances of bovine syncytial virus infection were found among normal and lymphosarcomatous cattle by immunodiffusion tests, with 21% of animals in normal herds showing infection, and 22% of lymphosarcomatous cattle showing infection.

- 1876 DETECTION OF A BOVINE VIRUS ASSOCIATED WITH SYNCYTIAL FORMATION IN MIXED CELL CULTURES. (E.) Cornefert-Jensen, F. (Sch. Vetr. Med., U. Pennsylvania, Philadelphia), N. D. Stock and R. R. Marshak. *Bibl Haemat* 36:453-464, 1970.

Human thoracic duct and peripheral blood lymphocytes from cattle with lymphosarcoma were co-cultivated with cultures of human diploid cells, embryonic bovine tracheal cells or bovine embryonic kidney cells, the lymphocytes from lymphosarcomatous cattle exhibited peripolesis and emperipolesis, attaching to and penetrating both human and bovine feeder cells. Peripolesis and emperipolesis became manifest on day 16 after the initiation of mixed cell cultures. Masked virus of uncertain type designated BSV was found in lymphosarcomatous bovine cells which produced a cytopathic effect in the feeder cells in mixed cell cultures; the cytopathic effect consisted of the formation of large syncytia, nuclear lobulation, microfragmentation, and cytoplasmic vacuolation. Co-cultivation of syncytia with normal bovine lymphocytes resulted in transfer of the cytopathic effect to the normal cells; however, none of the infected cell cultures yielded infectious virus. The original phenomena of cell attachment and penetration by

lymphosarcomatous cells may have played a role in the transfer of the viral genome from leukocytes to the feeder cells, the genome becoming reactivated upon entry into the feeder cells. Numerous virus-like particles could be seen in bovine cells cultures infected by co-cultivation with lymphosarcomatous lymphoid cells. Newborn calves of virus-infected animals did not carry BSV or BSV antibody; however, calves could be infected with BSV by injecting them with infected living cells from mixed cell cultures or with peripheral blood from infected cattle. None of the infected calves developed apparent lymphosarcoma. BSV infection was found to occur naturally in normal herds in approximately 4% of the cattle. The incidence of BSV infection was higher in adult cattle with lymphosarcoma (100% incidence) and in cattle herds with many cases of lymphosarcoma (92-98% incidence). Herds into which cattle from herds including lymphosarcomatous animals had been introduced showed a 35% incidence of BSV infection.

- 1877 ISOLATION OF C-TYPE VIRUS PARTICLES FROM LEUKEMIC AND LYMPHOCYTIC CATTLE. (E.) Dutta, S. K. (Coll. Vetr. Med., U. Minnesota, St. Paul), V. L. Larson, D. K. Sorensen, V. Perman, A. F. Weber, R. F. Hammer and R. E. Shope, Jr. *Bibl Haemat* 36:548-554, 1970.

Electron microscopic studies were carried out on the lymphocytes of cattle with leukemia and lymphocytosis to detect C-type virus particles in these cells. Lymphocytes from the affected animals, and from normal controls, were cultured and stimulated with phytohemagglutinin. Virus particles were observed in 72 hr phytohemagglutinin stimulated lymphocyte cultures; cultures with many immature lymphocytes had more virus particles. Particles were C-type, 100-110 mμ in diameter, and often were seen in the vicinity of cytoplasmic processes of lymphocytes. Particles were isolated from 5 of 7 leukemic cows and from 5 of 5 lymphocytotic cows; no particles were found in normal cows.

- 1878 RNA-DEPENDENT DNA POLYMERASE ACTIVITY IN VIRUS-LIKE PARTICLES ISOLATED FROM HUMAN MILK. (E.) Schlom, J. (Coll. Phys. Surg., Columbia U., New York, N. Y.), S. Spiegelman and D. Moore. *Nature* 231(5298):97-100, 1971.

Milk from American women with and without a familial history of breast cancer was examined for RNA-dependent DNA polymerase activity. Thirteen milk samples examined for type B particles and corresponding RNA-dependent DNA polymerase assays showed a positive correlation between the presence of these virus-like particles and the presence of polymerase activity.

- 1879 THE RATE OF CHROMOSOMAL ABERRATIONS IN HUMAN PERIPHERAL LYMPHOCYTES AFTER VACCINATION WITH VACCINIA-VIRUS *IN VIVO* AND *IN VITRO*. (Ger.) Baldauf, W. (Bavarian Immun. Inst., Munich, Germany), B. Stenglein, I. Unglaub-Leisten, H. Bulheller and H. Stickl. *Klin Wschr* 49(5):260-263, 1971.

Chromosomal abnormalities were induced in PHA-stimulated human lymphocytes from peripheral blood by inoculation of the cultures with vaccinia virus in concentrations of 10^4 and 10^5 plaque forming units/ml. Seven days after virus treatment, adult blood showed significantly increased numbers of chromosomal aberrations including chromatid aberrations, structural aberrations, deletions and dislocations. By 6 months after virus treatment, frequencies of chromosomal aberrations had returned to normal. Lymphocytes from children also showed increased incidence of chromosomal aberrations following vaccinia virus infection of cells *in vitro*; by 7 days after infection, chromosome aberrations had increased 100% over control.

- 1880 EVIDENCE FOR A VIRUS IN HUMAN SARCOMAS. (E.) Morton, D. L. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), F. R. Eilber, R. A. Malmgren and K. O. Cooke. *Bibl Haemat* 36:754-760, 1970.

Sera from sarcoma patients bearing a high titer of antisarcoma antibody were tested by complement fixation against a variety of tissue culture cells from normal and malignant human tissues. Sarcoma specific antigens were found in 10 of 11 cultures established from human sarcomas including osteosarcomas, liposarcomas, fibrosarcomas and synovial cell sarcomas. Most sarcomas had antigen titers of 1/40-1/160. Only 1 of 5 normal cell cultures contained sarcoma specific antigen. When sera from patients with sarcoma and their relatives, and normal sera were tested by complement fixation using antigen prepared from a liposarcoma, 95% of the patients with skeletal or soft tissue sarcomas had antibody to the liposarcoma antigen; only 20% of sera from normal subjects had this antigen. Antibody titers in relatives of sarcoma patients were intermediate between titers in sarcoma patients and titers in controls.

- 1881 CHARACTERIZATION OF DNA ISOLATED FROM METAPHASE CHROMOSOMES OF CELLS CONTAINING EPSTEIN-BARR VIRUS. (E.) Ludwig, H. (Baylor Coll. Med., Houston, Texas), N. Biswal and M. Benyesh-Melnick. *Biochim Biophys Acta* 232(2):261-270, 1971.

DNA was extracted from chromosomes isolated and fractionated from Burkitt's lymphoma cells grown in Eagle's medium supplemented with 20% fetal bovine serum; 5-10 μ g/ml of colcemide was added during the logarithmic growth phase. After 18 hr of incubation with colcemide, the fractions were pooled separately into 3 groups according to chromosome size. Thermal denaturation of DNA's from total chromosomes, chromosome fractions and interphase nuclei yielded a midpoint transition (T_m) in the range of 84-85°; these values corresponded to G+C contents of 36-38%. The nucleotide composition of the DNA from the fractionated chromosomes and the extrachromosomal DNA did not vary significantly from each other. The DNA of the total cell had a buoyant density of 1.698 g/cm³ which did not differ significantly from nuclear DNA of these cells treated with colcemide. However,

centrifugation revealed a small DNA peak with a buoyant density of 1.723 g/cm³ corresponding to a G+C content of 66% in 3 of 7 experiments; this peak represented 2-3% of the bulk chromosomal DNA and the highest amount was present in the small chromosomes. The density of this additional DNA corresponded to the value for DNA extracted from herpes simplex viral DNA which had a density of 1.725 g/cm³; this DNA may represent the Epstein-Barr virus DNA.

- 1882 EB VIRUS INFECTION AND PROPAGATION IN HUMAN HEMATOPOIETIC CELLS. (E.) Horoszewicz, J. S. (Roswell Park Mem. Inst., Buffalo, N. Y.), V. C. Dunkel, L. Avila and J. T. Grace, Jr. *Bibl Haemat* 36:722-738, 1970.

Epstein-Barr virus (EBV) was introduced into cultures of EBV-free cells from a human with myelogenous leukemia; the enveloped virus particles attached quickly to the cells; 8-12 hr after infection, viruses penetrated cell membranes in the manner of herpes simplex virus. Human leukemic cells were infected with low doses of EBV to establish a virus carrier state; a good correlation was found for concentration of virus and decline of viability in infected cultures. A virus carrier state was established in 45 cultures of EBV-free human leukemic cells and maintained for periods up to 2.5 yr. When hematopoietic cell lines from normal humans were infected with EBV, cell death ensued within 5 days postinfection with high concentrations of virus. In cultures infected with lower virus concentrations, virus-producing cells gradually disappeared. Sera which gave positive immunofluorescent reactions to EBV neutralized the virus; however, these sera did not impair the infection of cells already chronically infected with EBV. Infection with EBV resulted in the appearance of a new antigen on the surface of infected cells.

- 1883 LYMPHOPROLIFERATIVE EFFECT OF EPSTEIN-BARR VIRUS ON NORMAL HUMAN LYMPHOCYTES IN CULTURES. (E.) Gerber, P. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), J. Whang-Peng and J. H. Monroe. *Bibl Haemat* 36:739-750, 1970.

Leukocyte cultures were prepared from blood of a 21-yr-old male with no evidence of the presence of herpes viruses; viable cells disappeared from cultures at 50-65 days of cultivation. When the growth of virus-free cultures was compared with the growth of cultures infected with Epstein-Barr virus (EBV), it was found that virus-free cultures and cultures treated with EBV neutralized with EBV-positive human serum antibodies continued to lose viable cells after 21 days in culture, while cultures treated with non-neutralized EBV continued to proliferate and showed the development of macroscopic cell clusters. Virus-transformed cultures contained about 12% small lymphocytes, 70% medium-sized lymphocytes and 14% large lymphocytes; all lymphocytes had large nuclei and sparse cytoplasm. Virus-free cultures and cultures containing neutralized EBV failed to stain in immunofluorescence tests, while 10-15% of the

cells of EBV-infected cultures stained by about 6 wk in culture. Chromosome analysis of virus-free cultures showed that phytohemagglutinin-stimulated cells had the normal male karyotype with 2% breaks and 0.5% polyploidy. Virus-transformed cultures showed hyperploidy, the number of cells having 47-49 chromosomes increasing with time in culture.

- 884 INDUCTION OF CELLULAR DNA SYNTHESIS IN HUMAN LEUCOCYTES BY EPSTEIN-BARR VIRUS. (E.) Gerber, P. (Div. Biol. Standards, Natl. Inst. Hlth., Bethesda, Md.) and B. H. Hoyer. *Nature* 231(5297):46-47, 1971.

Leukocytes were prepared from heparinized blood of healthy adults and treated in culture with *Candida albicans* allergenic extract, UV radiation-inactivated or heat-inactivated Epstein-Barr virus (EBV), or viable EBV. From 3-12 days in culture, leukocyte DNA synthesis, as measured by uptake of ³H-thymidine, had increased from 3 to 63 cpm/(culture 10⁻³) in cultures treated with viable virus. In control cultures and cultures treated with inactivated virus, uptake of labeled thymidine remained near 3 cpm/(culture 10⁻³) throughout the duration of the experimental period. In cultures treated with *C. albicans* extract, tritiated thymidine uptake dropped from 127 to 20 cpm/(culture 10⁻³) between days 3 and 12. The ³H-thymidine incorporated into acid precipitable components in cells stimulated by EBV was predominantly non-viral, and the stimulation of cellular DNA synthesis by EBV was regarded as significant and unusual.

- 885 CYTOGENETIC STUDIES OF EB VIRUS-POSITIVE AND EB VIRUS-NEGATIVE LYMPHOBLASTOID CELL LINES. (E.) Macek, M. (Inst. Child Develop. Res., Charles U., Prague, Czechoslovakia), E. H. Seidel, J. T. Lewis, J. P. Brunschwig, I. Wimberly and M. Benyesh-Melnick. *Cancer Res* 31(3):308-321, 1971.

Sixteen lymphoblastoid cell lines (including 3 lines of Burkitt's lymphoma cells, 3 lines of acute leukemia cells, 8 lines of infectious mononucleosis cells and 2 lines of cells from normal donors) were maintained in culture for periods up to 61 months. Most cells retained a diploid mode with the exception of some infectious mononucleosis cells which developed complete heteroploidy, and some lines from all 4 classes developed hyperdiploidy with 47 or 48 chromosomes. Some of the common types of marker chromosomes were seen in all the 16 lines examined. The most frequent type was marker m₂, an abnormal chromosome similar to chromosome 18 but 34% larger than a normal A₂ chromosome. An abnormal chromosome with the centromere in the subtelocentric region was another frequently observed marker chromosome. Other abnormalities observed included chromosomes with the centromere in the terminal region, and long acrocentric chromosomes. An increased proportion of chromosomes with trisomy C was found in 11 of the 16 cell lines, with trisomy D and G also observed, but less often. Cells with marker chromosomes or trisomies appeared with increasing frequency in clones

of cultured cell lines, indicating that cells with these features have a selective advantage for growth *in vitro*. Epstein-Barr virus was found in cells from all of the 3 Burkitt's lymphoma lines, in 1 of the acute leukemia lines, and in 5 of the infectious mononucleosis lines. No virus was found in normal cell lines, and there did not appear to be a correlation between the presence of virus and any of the observed chromosomal features of the cell lines. Subterminal constrictions of the long arms of group C chromosomes were found in all but 1 cell line.

- 1886 STUDIES OF EPSTEIN-BARR VIRUS (E.) Grace, J. T., Jr. (Roswell Park Mem. Inst., Buffalo, N.Y.). *Ann NY Acad Sci* 174(2):946-966, 1970.

Continuing experiments are described in which clones of Burkitt lymphoma cells are examined for the presence of Epstein-Barr virus (EBV); a correlation was found between percent of fluorescent cells in immunofluorescence tests and percent of virus-containing cells; less than 3% of the cells drawn from a culture with 1% fluorescent cells contained virus, and 69% of the cells drawn from a culture having 75% fluorescent cells contained virus. Burkitt cells produced the fewest virus when cultured in regular growth medium at 37°; maximum virus counts were seen when cells were cultured at lower temperatures. Virus from these cells were usually solitary and only occasionally appeared in groups. Relatively few particles had envelopes. It was found that more than 90% of sera obtained from normal adults in the United States gave positive immunofluorescence when tested against virus-containing cell lines. Infectivity of EBV was found to rise with dose of virus, and infection resulted in severe cell damage with the appearance of a new antigen at the surface of infected cells. The progress of EBV infection resembled that of herpes simplex virus infection. No sign of infection could be detected when EBV was inoculated into cultures of various nonhuman cell systems.

- 1887 MINOR RNA AND OTHER COMPONENTS OF HOST ORIGIN INTRINSIC TO AVIAN LEUKOSIS VIRUS PARTICLES. (E.) Bolognesi, D. P. (Max Planck Inst. Virus Res., Tübingen, Germany) and T. Obara. *Bibl Haemat* 36:126-139, 1970.

Concentrated virus from leukemic plasma and labeled virus from tissue culture fluids were layered on a 20-50% discontinuous sucrose gradient, fractionated and assayed for optical density, radioactivity, and RNA analysis. The RNA pattern following isolation from a purified avian myeloblastosis virus preparation revealed a minor component sedimenting between the 60S and 4-5S RNA while fractionation of RNA from the latter co-sedimented with those of the former which were previously shown to co-sediment with ribosomal RNA. Ribonuclease treatment had little effect upon the proportion of 26S and 16S RNA and the base ratio analysis indicated that the viral and analogous cell components had corresponding base composition with a higher G-C content in the 26S ribosomal RNA.

- 1888 EVIDENCE FOR THE VERTICAL TRANSMISSION OF 'NON-INFECTIOUS' AVIAN LEUKOSIS VIRUS IN 'LEUKOSIS-FREE' CHICKENS. (E.) Sarma, P. S. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), F. Edwards, R. J. Huebner, H. C. Turner and L. Vernon. *Bibl Haemat* 36:168-182, 1970.

Chick embryo liver cells prepared from material taken from "leukosis-free" flocks of white leghorn chickens were tested by complement-fixation studies for the presence of complement fixing antigens and for the presence of infectious leukosis virus. Of 138 embryo liver cell samples tested, 53 gave complement fixing reactions positive for an antigen similar to the avian leukosis group specific antigen. Infectious avian leukosis virus was recovered from chick embryo liver fibroblast cultures but not from quail embryo liver fibroblast cultures. Virus isolated from chick embryo liver fibroblast cultures appeared to be identical to Rous-associated virus group 1. While liver samples from embryo derived from virus-transmitting hens failed to yield infectious virus, many of these same samples yielded ether-resistant complement fixing antigen. Chicken embryo liver antigens were found to be of 2 types: an ether-resistant antigen similar to the leukosis group specific antigen, and an ether-labile antigen which was probably a chicken isoantigen. Apparently a non-infectious avian leukosis virus is transmitted vertically or, alternatively, an infectious virus which has an extremely limited host range is transmitted.

- 1889 ENHANCING THE SUSCEPTIBILITY OF CHICKS TO MYELOID LEUKAEMIA VIRUS BY MYELOID-CELL STIMULATION. (E.) Lagerlöf, B. (Karolinska Hosp., Stockholm, Sweden). *Acta Path Microbiol Scand* 79(2): 208-209, 1971.

One-day-old chicks were given i.p. injections of 1×10^4 staphylococci; chicks developed acute peritonitis. Of the chicks injected with staphylococci, some were given a subsequent injection of pure or diluted BAI strain of myeloid leukemia virus. Chicks injected with staphylococci developed a higher incidence of leukemia after a shorter elapsed time from the injection of virus than did chicks injected with virus with no staphylococci pretreatment. Undiluted leukemia virus produced a 75% incidence of leukemia among pretreated chicks and a 40% incidence in untreated chicks on day 35 after virus inoculation. No difference in the severity of the leukemia developed by the staphylococcus-virus and the virus only group was found. The enhancing effect of staphylococcus infection on leukemogenesis was apparently due to the stimulation of the myeloid cells by the staphylococcus.

- 1890 TRANSMISSION OF AVIAN MYELOBLASTOSIS BY BAI STRAIN A VIRUS RIBONUCLEIC ACID. (E.) Veprek, L. (Duke U. Med. Ctr., Durham, N. C.), D. Beard, A. J. Langlois, R. Ishizaki and J. Beard. *J Natl Cancer Inst* 46(4):713-729, 1971.

Pellets prepared by centrifuging BAI strain A virus were treated with sodium dodecyl sulfate and dithio-

threitol to isolate the viral RNA, and high molecular wt RNA was used to infect chick embryo cells cultured with DEAE-dextran. Two of 5 RNA preparations induced infection, morphologic alteration, and liberation of virus by infected chick cells; a third preparation induced infection and synthesis of virus in cells but produced only 1 case of myeloblastosis when inoculated into newborn chicks. The other cell cultures infected with RNA preparations produced virus which, when inoculated into chicks, caused a characteristic BAI virus infection marked by myeloblastosis, and ovarian, renal and hepatic tumors. Nephroblastomas were also developed in some chicks. Virus produced by viral RNA-infected cultures transformed fresh chick embryo cells but did not transform bone marrow cells. RNA preparations inducing infection apparently contained no virus particles; the infection of chick cells by RNA could be prohibited by ribonuclease treatment. The infectious agent from BAI-RNA infected chick cells induced liberation of infectious virus in non-producer Rous sarcoma virus cells and interfered with Rous sarcoma virus and MC29 virus focus formation.

- 1891 VIROLOGICAL ANALYSIS OF INDIVIDUAL FOCI INDUCED IN HEMATOPOIETIC CELLS BY AVIAN MYELOBLASTOSIS VIRUS. (E.) Moscovici, C. (VA Hosp., Gainesville, Fla.). *Bibl Haemat* 36:148-152, 1970.

Chick embryo yolk sac cultures were infected with avian myeloblastosis virus of subgroups A and B. Foci of infected cells yielded myeloblasts containing virus; these myeloblasts induced cell transformation *in vitro* and leukemia in birds inoculated with them. Another group of cells produced foci which released myeloblastosis-associated virus; myeloblasts from these foci did not transform cells *in vitro*. When injected into living chick embryos, these cells did not produce leukemia, but did produce adenocarcinoma. Only 1 focus of 20 gave rise to infectious progeny after infection of yolk sac cultures with avian myeloblastosis virus subgroup B; cells from this focus had transforming ability and produced leukemia in inoculated birds. Virus-free foci were challenged with a variety of leukosis viruses including Rous-associated virus and myeloblastosis-associated virus and transforming avian myeloblastosis virus was rescued in some cases.

- 1892 DEOXYRIBONUCLEIC ACID POLYMERASE ACTIVITY ASSOCIATED WITH STRAIN MC29 TUMOR VIRUS. (E.) Weber, G. H. (Dept. Agric. Chem., Oregon St. U., Corvallis), A. A. Kiessling and G. S. Beaudreau. *J Virol* 7(2):214-220, 1971.

The presence of a DNA polymerizing activity in strain MC29 tumor virus was studied in infected chick embryo cells utilizing deoxyribonucleoside triphosphates and calf thymus DNA. DNA directed reactions had a 10-fold greater rate of ^3H -thymidine triphosphate incorporation compared to endogenous reactions; a strong depression in rate resulted from the omission of dATP and dCTP and a lesser depression was seen with the omission of dGTP. The enzyme preparation from

29 virus incorporated ^3H -dGTP into DNA at twice the rate of ^3H -TTP incorporation, whereas enzyme from avian myeloblastosis virus incorporated ^3H -dGTP at about 3 times the rate of ^3H -TTP incorporation. DNA synthesis with the MC29 virus preparation without added template showed only slight DNA synthesis relative to the activity when DNA was added. These results demonstrated clearly that a DNA-polymerase activity is associated with MC29 virus infection.

93 DNA POLYMERASE ACTIVITY IN HOMOGENATES OF CELLS INFECTED WITH MC29 VIRUS. (E.) Weber, H. (Dept. Agric. Chem., Oregon St. U., Corvallis), A. Kiessling and G. S. Beaudreau. *Biochem Biophys Commun* 42(6):993-999, 1971.

Chick embryo cells were infected with myelocytomatosis virus (2.8 x 10⁴ focus forming units/culture), and infected and uninfected cells were assayed for DNA polymerase. The enzyme was present in uninfected chick cells, but the activity in virus infected cells was greater than in uninfected cells. The homopolymer dU:dC:poly rG did not stimulate DNA polymerase in uninfected cells; however dC:rG produced a 3-fold stimulation of DNA synthesis in virus-infected cells. DNA from *M. lysisdeikticus* and from avian myeloblastosis virus produced greater DNA synthesis in virus infected cells than in uninfected cells.

94 FELINE LEUKEMIA: CHARACTERIZATION OF THE VIRUS. (E.) Burger, C. L. (St. U. New York, Upstate Med. Ctr., Syracuse), J. L. Olpin, G. Soofi and B. C. Maher. *Bibl Haemat* 36:379-386, 1970.

Line leukemia virus obtained from a cell line derived from a kitten inoculated with feline lymphocytic leukemia was separated by centrifugation and prepared for nucleic acid extraction, chemical determination, RNA and amino acid analysis. The maximum absorbency of the nucleic acid fraction occurred at 260 nm and the minimum at 230 nm; orcinol reactions confirmed the presence of RNA type nucleic acids. The melting profile suggested the RNA was a single-stranded type and it was converted to oligonucleotides by RNase. The buoyant density of the RNA (1.64 g/ml) was calculated by analytical ultracentrifugation; the band width when compared with that obtained in polyoma viral nucleic acid indicated a molecular wt of at least 1 x 10⁶. Electrophoretic migrations ranged from 45 min to 3 hr and cells labeled with tritiated uridine showed label exclusively in the nucleus after 1 hr, while later stages showed filtration into the cytoplasm. Not all cells at 1 time periods produced reasonable data.

95 GROWTH OF FELINE LEUKEMIA VIRUS IN HUMAN, CANINE AND PORCINE CELLS. (E.) Jarrett, (Anim. Leukemia Res. Unit, U. Glasgow, Scotland), M. Laird and D. Hay. *Bibl Haemat* 36:387-392, 1970.

Line leukemia virus (FeLV-5) was isolated from a cat with spontaneous alimentary lymphosarcoma and

maintained in cultures of feline embryonic cells. The virus was inoculated into cultures of porcine and canine kidney cells and human embryonic lung cells; the virus was found to be replicating in all recipient cell cultures by electron microscopy in the third wk after FeLV-5 infection. Complete viral particles with the character of leukemia viruses were seen in extracellular spaces in human cell cultures, and incomplete particles were seen budding from cell membranes. FeLV-5 did not appear to grow in bovine, murine, rat or chicken cells. Growth of virus was also demonstrated in human lung embryo cells by the incorporation of ^3H -uridine into purified virus from culture fluids.

1896 REPEATED DEMONSTRATION OF A MOUSE LEUKEMIA VIRUS AFTER TREATMENT WITH CHEMICAL CARCINOGENS. (E.) Ball, J. K. (Cancer Res. Lab., U. Western Ontario, London, Canada) and J. A. McCarter. *J Natl Cancer Inst* 46(4):751-762, 1971.

Although untreated CFW/D mice developed thymic lymphomas in only 0.12% of cases, the incidence of thymic tumors among mice given a thymic injection of cell-free filtrate from a 7,12-dimethylbenz(a)anthracene (DMBA)-induced thymic lymphoma was 73%; tumors induced by lymphoma cell-free filtrates had short latent periods (161 days average). When heavily (20,000 or 40,000 rads) irradiated tumor cell supernatants were injected into irradiated mice containing 7-day-old intrarenal thymus grafts, supernatants from 9 of 11 DMBA-induced lymphomas produced tumors in recipients. The supernatant from one of these tumors borne by a thymic grafted mouse, when injected into other mice, produced 7 tumors in 9 mice. Most tumors in thymic graft-bearing mice involved the grafted thymus only; irradiated supernatant was usually injected directly into the thymic graft. No significant leukemogenic activity was noted for thymus, bone marrow or liver taken from normal mice; thymus graft tumors did develop in 4 of 54 mice given whole-body irradiation and an intrarenal thymic graft. Seven days after a neonatal injection of DMBA, bone marrow and liver preparations from treated mice developed thymic lymphomas with low incidences. With serial animal passage, the tumor incidence increased and latency shortened. Thymic lymphomas could also be induced by injecting thymic grafted mice with supernatants from DMBA-induced fibrosarcomas and methylcholanthrene-induced fibrosarcomas. A thymic lymphoma, induced by passage of cell-free material from a DMBA-induced tumor, yielded a filtrate which could rescue the murine sarcoma virus genome present in Moloney sarcoma virus-induced hamster tumor cells.

1897 HEMOGLOBIN SYNTHESIS IN MURINE VIRUS-INDUCED LEUKEMIC CELLS IN VITRO: I. PARTIAL PURIFICATION AND IDENTIFICATION OF HEMOGLOBINS. (E.) Scher, W. (Mount Sinai Sch. Med., City U. New York, N. Y.), J. Gilbert Holland and C. Friend. *Blood* 37(4):428-437, 1971.

After at least 3 biweekly passages in medium containing radioactive iron, smears were prepared from cloned cultures of a mass-cultured Friend virus-

induced leukemic cell line, designated C-1A which had been in serial passage for over 4 yr. Iron accumulation and heme biosynthesis were assayed by the method of Krantz and Fried. Iron accumulation continued for 4 days in a cloned line (III-1) which produced a relatively high percentage of benzidine-positive cells, but it ceased to accumulate in the parent cells, C-1A, after 40 hr. When the rate of iron incorporation into heme in these 2 cell lines was compared, the difference became more striking. A rapid rate of iron incorporation into III-1 cells was maintained for 4 days, but ceased by the second day in C-1A cells. Hemoglobin isolated from 2 cloned lines after 72 hr of growth was resolved into 3 components on 10% polyacrylamide gel electrophoresis. The electrophoretic pattern of these 3 hemoglobins appeared similar to that of hemolysates of adult DBA/2J mice, from which the cells originated.

- 1898 STUDIES ON FRIEND VIRUS-INDUCED VIREMIA IN LETHALLY IRRADIATED MICE WITH OR WITHOUT HEMATOPOIETIC REPOPULATION. (E.) Rossi, G. B. (Mt. Sinai Sch. Med., City U. New York, N.Y.), E. De Harven, J. R. Haddad and C. Friend. *Int J Cancer* 7(2):303-312, 1971.

The effect of repopulating lethally irradiated ICR/Ha Swiss and DBA/2J mice with normal cells on Friend virus-induced viremia was studied in spleen and thymus cells under the electron microscope. Virus titers in the plasma of non-irradiated controls reached expected levels from day 4 on, while no appreciable amount of virus was recovered from the plasma of irradiated mice. Pellets from controls contained large populations of typical virus particles of the C and A type, whereas those from irradiated mice showed a variety of minute cell debris and platelet granules but no clearly identifiable virus particles. Viral replication in lethally irradiated mice inoculated with spleen cells and bone marrow was seen as confluent colonies in the spleen by the 10th day with only rare minute-sized colonies appearing in thymus cell-inoculated animals, including both erythroid and myeloid components. These data suggest that Friend leukemia virus replication is not supported by recipient mice deprived of practically all of their hematopoietic cells.

- 1899 INFLUENCE OF SENSITIZATION WITH BACTERIAL ANTIGENS ON THE REPLICATION OF FRIEND SPLEEN FOCUS-FORMING VIRUS. (E.) Flickinger, J. T. (C.H.U., U. Sherbrooke, Quebec, Canada) and J. M. Gentile. *Canad J Microbiol* 17(4):481-486, 1971.

Female mice of strain HA/ICR were given i.p. injections of 25 µg of O and H antigens prepared from *Salmonella typhosa* or *Proteus mirabilis*; the bacterial antigens were administered either 5 or 3 days before infection of mice with Friend virus, or simultaneously with virus infection, or 3 days after virus infection. Mice sensitized with *S. typhosa* antigens 5 days prior to virus infection showed an enhanced rate of Friend virus replication in the spleen com-

pared to mice sensitized 3 days before or 3 days after virus infection. On day 14 after virus infection, foci per spleen counts in mice given *S. typhosa* antigen 5 days before infection were increased over counts for mice given antigen 3 days before and 3 days after infection. The foci per spleen counts for mice in the latter 2 groups were similar to those recorded for mice not treated with bacterial antigen. In mice which were given both Friend virus and bacterial antigen simultaneously, virus replication was seen to be inhibited by day 14 postinfection. Treatment of mice with the H or flagellar antigen prepared from *P. Mirabilis* did not affect the replication of Friend virus in these mice, regardless of the time at which the antigen was administered relative to the time of virus infection.

- 1900 DEFECTIVE FRIEND SPLEEN FOCUS-FORMING VIRUS PSEUDOTYPE NEUTRALIZATION BY HELPER-SPECIFIC ANTISERA. (E.) Eckner, R. (Dept. Exp. Biol., Roswell Park Mem. Inst., Buffalo, N. Y.) and R. A. Steeves. *Nature* 229(8):241-243, 1971.

Spleen focus-forming virus was prepared from splenic homogenates of Friend virus-infected Ha/ICR swiss mice and injected into the lateral tail veins of untreated animals and of animals treated with 2 mg of hydrocortisone injected i.p. 9 and 8 days before infection and 1 mg 7 and 6 days before infection. The spleen focus-forming virus maintained in Swiss mice routinely gave single-hit dose-response titration patterns in susceptible hosts, but multiple hit patterns in BALB/c mice and other partially resistant strains. In treated mice, the injection dose-response curve shifted upward with no change in slope from that obtained with untreated mice. Upon co-infection with the 334C virus of Buffte and a lymphatic leukemia virus, the titers of the spleen focus-forming virus were greatly increased and the most elevated titers at the greatest dilution changed the slopes of the dose-response curves to a single hit form. In the presence of sera from Swiss mice given 10 weekly i.p. injections of Swiss lymphoma cells induced by a helper virus and leukemia virus, altered antigenicity of the spleen focus-forming virus pseudotypes resulted.

- 1901 NUCLEOSIDE DEAMINASE ACTIVITY IN VIRAL LEUKEMIA. (E.) Rothman, I. K. (New York U. Sch. Med., New York, N.Y.), V. G. Malathi and R. Silber. *Cancer Res* 31(3):274-276, 1971.

Swiss-Webster and BALB/c mice were inoculated with preparations of Friend leukemia virus, Rauscher leukemia virus, or Moloney virus and homogenates prepared from their spleens were examined for nucleoside deaminase activity measured by the amount of radioactively-labeled uridine formed by the deamination of ¹⁴C-labeled cytidine. A 10-fold increase in spleen wt was seen 5 days after infection with Friend virus. Control mice not injected with virus showed spleen nucleoside deaminase activity levels ranging from 2.6-3.8 milliunits/g spleen tissue. Nucleoside deaminase activity of mice infected with Friend virus was at 1013.0 milliunits/g by 8 days

postinfection, and nucleoside deaminase activity in mice infected with Rauscher virus was at 389 milliunits/g by 18 days postinfection. Administration of 50 mg phenylhydrazine in the absence of viral infection elevated nucleoside deaminase activity to 294 milliunits/g by 4 days after injection of phenylhydrazine. Infection with Moloney virus produced nucleoside deaminase levels of 6.5 milliunits/g by 5 days postinfection. The erythroid nature of the disorders induced by Friend and Rauscher viruses may be related to the elevated nucleoside deaminase activity.

02 PROPERTIES OF TRANSFORMED HEMOPOIETIC CELLS IN MICE INFECTED WITH THE FRIEND VIRUS COMPLEX. (E.) Steeves, R. A. (Roswell Park Mem. Inst., Buffalo, N.Y.), E. A. Mirand and S. Thomson. *Bibl Haemat* 36:624-633, 1970.

Young adult BSF₁ hybrid mice were injected i.v. with Friend virus-infected Swiss inbred mice spleen cells; after the injection the spleen cells from the hybrid primary recipients were suspended in medium and assayed for tumor colony forming units in hybrid secondary recipients. Ten days after injection, the frequency of tumor colony forming units was one per 10⁴ spleen cells with a decline noted during the next 10 days, while total cell count per spleen rose slowly. To demonstrate the presence of a neoantigen on Friend virus-induced tumor colony forming units, BSF₁ mice were injected i.p. 20 or 4 days before cell challenge with normal Swiss inbred mice spleen cells, cellular antigen from Friend virus-infected and normal Swiss inbred mice, or Friend virus complex. Nine days after challenge with Friend cells, the only groups which showed significant transplantation immunity were those injected with cellular antigen from virus-infected mice or with an ether-extracted Friend virus complex. γ-irradiated Friend virus complex failed to induce this immunity.

03 EFFECT OF BCG ON FRIEND DISEASE VIRUS IN MICE. (E.) Larson, C. (Dept. Microbiol., U. Montana, Missoula), R. Ushida, M. Florey, R. Baker and M. Baker. *Nature* 229(53):243-244, 1971.

Sixty-five female mice were infected with Friend disease virus (FDV) by i.v. injection of 0.3 ml of virus preparation; 31 of the mice had, 3 wk previously, been immunized with *Mycobacterium bovis* (BCG). After 4 wk, FDV-infected mice had pronounced splenomegaly compared to BCG-immunized mice. At 8.5 wk postinfection, 50% of the unimmunized mice and 23% of the immunized mice had died; mortality at 12.5 wk among immunized and unimmunized mice was 50% and 90%, resp. In a related experiment, male mice were immunized with BCG and later challenged with FDV. Sixteen wk after infection, mortality in immunized and unimmunized mice was 50% and 100%, resp. It is believed that the effect of BCG vaccination on subsequent FDV infections is based on nonspecific cellular immunity.

1904 THE ROLE OF GENETICS IN GROSS VIRUS LEUKEMOGENESIS. (E.) Lilly, F. (Albert Einstein Coll. Med., Bronx, N. Y.). *Bibl Haemat* 36:213-220, 1970.

Hybrid (BALB x C57BL) x BALB backcross generation mice and mice of the (B10.BR x C57BL) x N10.BR backcross generation inoculated with Gross virus and typed for the histocompatibility-2 locus of the 9th chromosome were observed for leukemia incidence. Heterozygous H-2^b/H-2^d mice among the first hybrids showed a lower incidence of leukemia among 2 groups with values of 3% and 37% compared to their homozygous H-2^d/H-2^d littermates with values of 44% and 76%. Among the second hybrids the H-2^k/H-2^k segregants showed a leukemia incidence that was consistently higher and occurred sooner than that among heterozygous H-2^k/H-2^b segregants; however, the difference between the 2 classes of mice appeared greater when virus preparations of lower potency were used than when high-titer preparations were used. The incidence of leukemia induced by Gross virus among mice of various strains indicated a significantly greater susceptibility to leukemogenesis among BALB/c strain mice than mice of the A strain and presented a more complex association between the histocompatibility locus and leukemogenesis.

1905 STUDIES ON HYPODIPLOID AND HYPERDIPLOID VIRUS-INDUCED MOUSE LEUKEMIAS AND THE VERTICAL TRANSMISSION OF MSV-MOLONEY. (E.) Ida, N. (Toyo Kogyo Hosp., Hiroshima, Japan), Y. Ikawa and Y. Ohba. *Bibl Haemat* 36:221-233, 1970.

Thirty-nine C3H mice were examined from the 3rd through the 16th transplant generation of Moloney virus-induced mouse leukemia with a high percentage of the cells derived from their thymuses, spleens, mesenteric lymph nodes and livers showing predominantly 39 acrocentric chromosomes compared to the 40-chromosome complement of the control tissue. New-born Swiss mice inoculated at birth with cell-free supernatants of murine virus-induced sarcomas harvested before the 30th day of culture revealed development of sarcomas in 100% of 34 recipients, while supernatant of a 33-day culture produced sarcomas in only 41% of the recipient hosts with latent periods of 85 days. In addition, leukemias developed in 29.4% of the mice, revealing a hyperdiploid stemline with 41 chromosomes. Pregnant Swiss ICR mice repeatedly injected i.p. with murine sarcoma virus or with murine sarcoma virus and Moloney leukemia virus developed no tumors when virus-injection was initiated before or soon after the placenta was established or at the 9th day of gestation. One recipient of both viruses on the 13th gestation day developed a sarcoma after a latent period of 20 days and all recipient hosts receiving tissue culture fluid from this passage developed sarcomas.

1906 DECREASE IN TUMOR-PRODUCING CAPACITY OF MOUSE CELL LINES FOLLOWING INFECTION WITH MOUSE LEUKEMIA VIRUSES. (E.) Barbieri, D. (Inst. Gustave Roussy, Villejuif, France), J. Belehadek, Jr. and G. Barski. *Int J Cancer* 7(2):364-371, 1971.

Cell lines from C57BL/6 mice treated with 3-methylcholanthrene (3-MC) and from mice in which spontaneous tumors arose were infected in culture with Rauscher leukemia virus of a highly leukemogenic strain (RRL⁺) or with Rauscher virus of a mildly leukemogenic strain (RCL⁻). While both the 3-MC-treated mouse cells and the spontaneously-transformed mouse cells alone produced tumors in syngeneic mice, the tumorigenicity of these cells was seen to decline following *in vitro* infection with Rauscher virus. When injected into mice, the virus-infected spontaneously-transformed cells produced tumor takes in 23-54% of cases as compared to 100% takes observed for non-infected spontaneously transformed cells. Latency of tumor appearance in mice inoculated with spontaneously transformed cells increased from 35 days to 164-165 days upon infection of the cells with Rauscher virus. When Rauscher virus-infected spontaneously transformed cells were inoculated into mice which had been pre-immunized by prior injection of the same cell and subjected to whole-body X-irradiation (400 r), 73% of the irradiated but unimmunized mice developed tumors; none of the immunized and irradiated mice developed tumors. Mice inoculated with cells from 3-MC-treated tumor bearing mice developed tumors in 100% of the cases, but mice inoculated with 3-MC-transformed cells infected with RRL⁺ or RCL⁻ virus did not develop tumors. In all cells infected with Rauscher virus C-type virus particles appeared in the infected cell cultures; a surface antigen reacting with anti-Rauscher virus serum also appeared in virus-infected transformed cells. When spontaneously-transformed mouse cells were treated with 3-MC, C-type particles and an anti-Gross leukemia virus surface antigen were observed in the cultures. Treatment of spontaneously-transformed cells with 3-MC produced cells which were less tumorigenic than untreated transformed cells.

- 1907 ENZYME STUDIES IN EXPERIMENTAL LEUKEMIA. (E.) Cory, J. G. (Dept. Chem., U. South Florida, Tampa) and M. A. Rich. *Bibl Haemat* 36:267-277, 1970.

The content in mouse liver, spleen and thymus of enzymes involved in the degradation of nucleic acids was altered in mice infected with Rauscher or Rich leukemia viruses. Enzymes were assayed in normal and virus-infected organs at 3, 6 and 14 days after inoculation of virus, and results were expressed as the ratio of specific enzyme activities. In the spleen, aspartyl transcarbamylase (ATCase) activity was increased in Rauscher-infected mice, ratios of enzyme in infected and normal mice being 1:30 and 3:0 on day 6 and 14, resp. RNase and alkaline phosphatase activity were reduced in spleens of Rauscher virus-infected animals. ATCase increased 10-fold in Rauscher-infected mouse thymus by 3 days postinfection; infected mouse thymus also showed 3-fold increases in acid RNase and in phosphodiesterase. Rich virus infection also produced similar changes in thymus, liver and spleen enzyme activities.

- 1908 HIGH AND LOW LEUKEMOGENIC VARIANTS OF RAUSCHER VIRUS HAVING A COMPARABLE INFECTIVITY *IN VITRO*. (E.) Barski, G. (Inst. Gustave

Roussy, Villejuif, France). *Bibl Haemat* 36:323-326, 1970.

Cell lines derived from lung tissue of adult C57BL mice were infected with variants of Rauscher leukemia virus having high (Le⁺) and low (Le⁻) leukemogenicity. Both virus variants produced C-type virus particles in transformed cells, and both variants showed similar indices of specific cell immunofluorescence. The 2 variants performed alike in specific cytotoxicity tests. Dilutions of Le⁺ and Le⁻ variants were of similar infectivity *in vitro*. However, when cultures of Le⁺ and Le⁻ virus were subjected to ultracentrifugation and their supernatants inoculated into newborn BALB/c mice, Le⁺ supernatants produced leukemias in nearly all inoculated animals, while Le⁻ supernatants gave no leukemias, the difference in leukemogenic potential between Le⁺ and Le⁻ viruses amounting to 5 logs. Apparently, the attenuation of the leukemogenic properties of Le⁻ virus was not due to the lowering of virus production in cultures infected with this virus variant, nor to a decline in cell infectivity of Le⁻ but was due to an inherent low pathogenic potential.

- 1909 TESTS FOR MOUSE LEUKEMIA VIRUSES AND ISOLATION OF SOME OF THEIR COMPONENTS. (E.) Schäfer, W. (Max Planck Inst. Virus Res., Tübingen, Germany), J. Szanto, F. A. Anderer, H. Frank, H. Gelderblom, J. Lange and L. Pister. *Bibl Haemat* 36:327-332, 1970.

A group-specific antigen was isolated from Friend and Rauscher murine leukemias by complement fixation tests the specific activity of the antigen was very high, corresponding to 10⁻⁹ to 10⁻⁸g of protein per positive complement fixation. A hemagglutination reaction, using sheep red blood cells, was produced for the virus only when some host material was removed from the virus by treatment with neuraminidase and phospholipidase C; in the presence of these enzymes, hemagglutination titers of 1,024 were attained. For positive hemagglutination reactions, 3 x 10¹⁰ Rauscher virus particles were needed. The hemagglutinin appeared to be a virus-specific constituent of the murine leukemia virus particles having a type specific antigenic character.

- 1910 EVIDENCE FOR THE RAPID DECREASE IN LEUKEMOGENIC POTENTIAL OF RAUSCHER LEUKEMIA VIRUS IN CELL CULTURE. (E.) Schlom, J. (Coll. Phys. Surg. Columbia U., New York, N.Y.), J. B. Moloney and V. Groshen. *Cancer Res* 31(3):260-264, 1971.

Mice were inoculated with Rauscher leukemia virus and the amount of virus required to produce spleen weight increase (the "effective dose" or ED₅₀) was compared with titers of *in vitro* murine sarcoma helper virus in 6-day Rauscher virus cultures derived from inoculated mice; a constant ratio of about 10 murine sarcoma virus helper units to 1 splenomegaly ED₅₀ unit was found. Quantitative change in the virulence of Rauscher virus, as measured by the increased titers of murine sarcoma helper virus in Rauscher virus cultures, were seen following single passages in culture of Rauscher virus.

Lysates derived from secondary mouse embryo fibroblast cultures 4 and 13 days after inoculation with Rauscher virus showed murine sarcoma virus helper unit titers 6300 times greater than the titers reflecting the leukemogenic activity of the sample (e.g., splenomegaly ED₅₀). Growth curves of Rauscher virus showed production of leukemogenic virus by 2 days postinfection, and maximum production of infectious virus occurred at day 5. By 24 hr postinfection, large quantities of murine sarcoma virus helper could be seen in the cultures. Following 1 passage in culture, the leukemogenicity of Rauscher viruses was seen to decline.

- 1911 INITIATION OF MAMMALIAN VIRAL PROTEIN SYNTHESIS. (E.) Caffier, H. (Inst. Molec. Virol., St. Louis U. Sch. Med., Mo.), H. Raskas, J. Parsons and M. Green. *Nature* 229(8):239-241, 1971.

Cytoplasmic extracts of cultured human cells (KB) infected with human adenovirus type 2 and labeled for 5 min with ³H-methionine were prepared; unlabeled cytoplasmic extracts from KB cells were incubated for 20 min with ³H-methionine for N-terminal amino-acid determination of nascent and released polypeptides. Nascent chains labeled under both conditions contained approximately 25% N-terminal methionine. The methionine incorporated into released proteins both *in vivo* and *in vitro* was 5% N-terminal, suggesting that methionine is an initiator amino-acid for adenovirus structural proteins.

- 1912 STRUCTURAL PROTEINS OF ADENOVIRUS: V. SIZE AND STRUCTURE OF THE ADENOVIRUS TYPE 2 HEXON. (E.) Franklin, R. M. (Wallenberg Lab. U. Uppsala, Sweden), U. Pettersson, K. Akervall, B. Strandberg and L. Philipson. *J Molec Biol* 57(3):383-395, 1971.

The adenovirus type 2 hexon was purified for molecular wt determination by means of sedimentation-diffusion and equilibrium sedimentation (hydrogen exchange with tritiated water); crystal density was determined by means of equilibration between buffer solution and bromobenzene and xylol. The molecular wt range obtained by sedimentation equilibrium (333,000 to 356,000) agreed well with the range determined from the crystallographic parameters (333,000 to 356,000); these values were slightly higher than those obtained from hydrodynamic data (313,000 to 333,000). The hexon crystallized into a bipyramidal-shaped crystal and the unit cell was cubic with $a = 149.9 \text{ \AA}$. The space group was $P2_13$ and there were 4 hexons/unit cell, 12 crystallographic asymmetric units/unit cell or 3 crystallographic units/hexon, each with a molecular wt of 110,000 to 119,000.

- 1913 CHARACTERIZATION OF CRYSTALS OF TYPE 5 ADENOVIRUS HEXON. (E.) Cornick, G. (Dept. Biophys., U. Chicago, Ill.), P. B. Sigler and H. S. Ginsberg. *J Molec Biol* 57(3):397-401, 1971.

Type 5 adenovirus hexon crystals were prepared by dialysis and mounted in thin-walled quartz capil-

laries containing stabilizing supernatant solution for X-ray diffraction; patterns were photographed and crystal densities were determined pycnometrically. The crystal structure was found to be isomorphous with type 2 and belonged to the cubic space group $P2_13$ with $a=b=c=149.9 \text{ \AA}$. In the asymmetric unit the calculated mass was $83,000 \pm 8000$ daltons and the volume fraction was 0.37 ± 0.03 . It is suggested that the asymmetric unit is 1/3 of the hexon.

- 1914 DEFECTIVE VIRIONS IN HUMAN ADENOVIRUS TYPE 12. (E.) Mak, S. (Dept. Biol., McMaster U., Hamilton, Ontario, Canada). *J Virol* 7(4):426-433, 1971.

Oncogenic human adenovirus type 12 and adenovirus type 2 were propagated in human cells in suspension, purified by cesium chloride equilibrium centrifugation and subsequently labeled with ¹⁴C-thymidine; the virus was added to a human epithelial cell line which was assayed for T-antigen and intranuclear inclusion body induction. Centrifugation in cesium chloride density gradients revealed 2 bands derived from adenovirus type 12 with a difference of 0.003 g/ml, indicating a difference in DNA content of 3-4%. A difference of 0.009 g/ml between the densities of type 2 and type 12 were observed, indicating a difference in DNA content of 8%. The number of virions added to give 37% survival (on the average one unit per cell) was about 150 to 300 for cell killing and about 3,000 to 10,000 for T-antigen induction; the lighter fractions had a much reduced specific infection compared to the virions of the heavy band of type 12, which showed a 7-10-fold higher specific infectivity. The T-antigen induction efficiency was similar within each virus preparation. Isopycnic centrifugation failed to reveal a significant generation of light virions in response to infection of cell with the heavy fractions after 2 passages in human cells. The oncogenicity of the defective virion is not known at present.

- 1915 PATHOLOGICAL RESPONSE OF THE CHICKEN EMBRYO TO AN AGENT WHICH CAUSES ACUTE LEUKOSIS (MAREK'S DISEASE). (E.) Evans, D. L. (M. D. Anderson Hosp. Tumor Inst., U. Texas, Houston), L. T. Patterson and J. N. Beasley. *Appl Microbiol* 21(2):321-326, 1971.

Detection of Marek's disease and the characteristics of the infecting agent were studied in the chicken embryo by means of microscopic techniques. Gross pathological appearance of small foci to gradually converging perilobular lesions with hepatomegaly, small granular-appearing white foci on the surface of the spleen with splenomegaly and liver discolorations, and thickenings of the chorioallantoic membrane with the appearance of small, white, granular clumps characterized the observed changes in the embryo. Microscopically, areas of focal necrosis occurred in the liver with no evidence of inflammatory reactions but with proliferation of lymphocytes and granulocytes in the liver and reticuloendothelial cell hyperplasia in the spleen. Changes occurred 3-4 days post-inoculation, and the agent was recovered from dander and feather follicles of 1-day-old infected chickens.

- 1916 SITE OF REPLICATION OF MAREK'S DISEASE VIRUS. (E.) Nazerian, K. (Reg. Poultry Res. Lab., East Lansing, Mich.). *Bibl Haemat* 36:210-212, 1970.

Two wk after inoculation of chickens with Marek's disease virus, virus particles were recovered from the feather follicles and from kidney cell cultures; birds had no gross lesions at the time of virus recovery. Higher virus yields were obtained from feather follicles than from kidney cells by the time that the chickens developed frank lesions. The virus particles which were recovered had the morphology of herpes virus, and 80% of the viruses had an outer envelope. Viruses were found in epithelial cells from feather follicles but not in epidermal cells, and they produced a cytopathic effect in cell cultures. Apparently, the feather follicle is the site of fully infectious Marek's disease virus in infected birds.

- 1917 HERPESVIRUS SAIMIRI INDUCED MALIGNANT LYMPHOMA: RECOVERY OF THE VIRAL AGENT FROM THE FATALY AFFECTED ANIMALS. (E.) Melendez, L. V. (Harvard Med. Sch., Southboro, Mass.), M. D. Daniel and R. D. Hunt. *Bibl Haemat* 36:751-753, 1970.

Three owl monkeys (*Aotus trivirgatus*) were inoculated i.m. with 3160 TCID₅₀ herpesvirus saimiri; 19-21 days thereafter the animals became moribund and were killed. Autopsy confirmed that the animals had died of reticulum cell malignant lymphoma. Herpesvirus saimiri was isolated from kidney tissues of these monkeys, and the 200 nm filtrate was inoculated i.m. into owl monkeys, causing the recipient monkeys to become moribund by day 17 postinoculation. Inoculation of 3 cotton-top marmoset monkeys (*Saguinus oedipus*) with herpesvirus saimiri produced similar results to those obtained in owl monkeys. Herpesvirus saimiri was isolated from kidney culture of 1 of the lymphomatous monkeys.

- 1918 HERPESVIRUS SAIMIRI: *IN VITRO* SENSITIVITY TO VIRUS-INDUCED INTERFERON AND TO POLYRIBOINOSINIC ACID:POLYRIBOCYTIDYLIC ACID. (E.) Barahona, H. H. (Harvard Med. Sch., Southboro, Mass.) and L. V. Melendez. *Proc Soc Exp Biol Med* 136(4): 1163-1167, 1971.

When owl monkey kidney cells were treated with Newcastle disease virus interferon prior to infection with herpesvirus saimiri, it was found that there was a delay of 24-48 hr in the onset of the cytopathic effect in cultures pretreated with interferon for 6 hr compared with virus-infected cultures not treated with interferon. The cytopathic effect was delayed by 6-7 days in cultures in which interferon was retained in the culture after virus infection. In both interferon-treated cultures, the cytopathic effect was reduced compared to control cultures. When polyriboninosinic acid:polyribocytidylic acid (poly I:C) was incubated with owl monkey kidney cells prior to infection, the herpesvirus saimiri cytopathic effect on the cultures was inhibited by 81%; at

concentrations of 10 µg/ml, poly I:C's protection of cells against viral damage was not constant. The protective efficacy of poly I:C was enhanced nearly 20% by the addition to the incubation medium of DEAE dextran in amounts of 50 µg/ml. When owl monkey cells were infected with herpesvirus saimiri and treated 1 hr postinfection with poly I:C and DEAE-dextran, no visible plaques appeared in the infected cultures, showing 100% inhibition of herpesvirus saimiri cytopathic effect.

- 1919 HERPESVIRUS SAIMIRI: III. PLAQUE FORMATION UNDER MULTI AGAR, METHYL CELLULOSE AND STARCH OVERLAYS. (E.) Daniel, M. D. (Harvard Med. Sch., Southboro, Mass.), H. Rabin, H. H. Barahona and L. V. Melendez. *Proc Soc Exp Biol Med* 136(4): 1192-1196, 1971.

Herpesvirus saimiri was inoculated into cultures of the following cell types for observation of plaque forming capacity: early and continuous passage owl monkey kidney cells, early passage marmoset kidney cells, early and continuous squirrel monkey kidney cells, continuous passage African green monkey kidney cells, and early passage fetal squirrel monkey heart, lung and intestine cells. Plaques developed under all experimental conditions in all cell types except African green monkey kidney cells and continuous squirrel monkey kidney cells; plaques in all cultures were of varying sizes. Squirrel monkey heart cells were the most susceptible to plaque induction by herpesvirus saimiri, being 4 times as susceptible as all the other cells. Harvests of single plaques produced heterogeneous plaques on serial plating. Plaques developed under all solidifying agents tested; the highest plaque counts were seen under methyl cellulose (mean plaque count of 60) while the mean plaque count with starch was 46. Protamine sulfate and, to a lesser extent, DEAE-dextran stimulated plaque production under agar, while arginine had no effect. The number of plaques was directly proportional to the virus dilution and to the volume of the virus inoculum.

- 1920 THE ASSOCIATION OF HERPES-LIKE VIRUS AND GUINEA PIG LEUKEMIA. (E.) Hsiung, G. D. (VA Hosp., West Haven, Conn.) and L. S. Kaplow. *Bibl Haemat* 36:578-583, 1970.

Herpes-like virus was isolated from minced kidney, liver, spleen and lung tissues of leukemic and non-leukemic strain 2 guinea pigs, a strain uniquely susceptible to an acute lymphoblastoid leukemia. Other guinea pig strains, including Hartley and Muta also harbored herpes-like virus. Herpes-like virus could not be isolated from supernates of tissue extracts, nor was it detected in electron microscopic examination of tissues taken directly from the strain 2 guinea pigs. Neutralizing antibodies to herpes virus were detected in all guinea pigs which harbored herpes-like virus, and in none of the guinea pigs examined which did not harbor herpes-like virus. C-type virus particles have also been observed in guinea pig

with leukemia, and it was thought that herpes-like viruses may act to complete the leukemogenic effect of C-type virus particles in leukemogenesis in strain 2 guinea pigs.

- 1921 THE INFLUENCE OF INHIBITORS OF MACROMOLECULAR SYNTHESIS ON CAPACITY OF HERPES SIMPLEX VIRUS TO INDUCE CHROMOSOMAL DAMAGE. (E.) Donner, L. (Czechoslovak Acad. Sci., Prague) and E. Gönzööl. *J Gen Virol* 10(3):243-250, 1971.

The effect of actinomycin D, puromycin and cytosine arabinoside on the capacity of herpes simplex virus isolated from human vesicular fluid of simple labial herpes maintained by passages on L cells was studied utilizing karyological analysis. The frequency of chromosomal aberrations in response to colchicine in control cells was 2% compared to 27-38% in infected cells with 2 types of lesions occurring in infected cultures as either chromosomal gaps and breaks or diffuse chromosomal lesions. When Actinomycin D was added either at the time of infection or 1 hr later, chromosomal damage did not result; when it was added 3 or 5 hr after infection, the frequency of chromosomal aberrations in infected cultures was not inhibited; similar results were obtained with treatment with puromycin. However, cytosine arabinoside treatment revealed 88-92% of metaphase in L cells having severe diffuse chromosomal lesions which appeared to be due to partial despiralization, erosion and/or extensive fragmentation of chromosomes, while control cells showed a relatively high incidence of metaphase plates with chromatid and isochromatid breaks but no diffuse chromosomal lesions. Results support the view that chromosomal changes induced by viruses are probably due to the action of early enzymes controlled by virus genes.

- 1922 RELATIONSHIP BETWEEN HERPES-TYPE VIRUS, CHINESE NASOPHARYNGEAL CARCINOMA AND AFRICAN LYMPHOMA. (E.) De-The, G. (Internat. Agency Res. Cancer, Lyon, France). *Bibl Haemat* 36:715-721, 1970.

Ultrastructural examination of cell cultures prepared from affected tissues of patients with nasopharyngeal carcinoma revealed the presence of herpes-type virus (HTV) capsids, nucleocapsids and extracellular virions, often attached to the cell surface. In addition, nasopharyngeal carcinoma cells were found to contain Epstein-Barr virus (EBV) type structural antigens and EBV related membrane reactive antigens. Eighty-four percent of nasopharyngeal carcinoma patients had high titers of EBV-type antibodies, while 10% of normals had EBV antibodies. The proportion of patients' sera having a high EBV antibody titer in nasopharyngeal cancer was similar to that in Burkitt's lymphoma. It appeared that HTV played some causal role in the EBV-associated development of nasopharyngeal carcinoma and Burkitt's lymphoma.

- 1923 STUDIES ON THE GROWTH OF HERPES SIMPLEX VIRUS IN LYMPHOBLASTOID CELLS. (E.) Floyd, R. (Baylor Coll. Med., Houston, Tex.), R. Glasser, V. Vonka and M. Benyesh-Melnick. *Acta Virol* 15(2):133-142, 1971.

Two Burkitt lymphoma cell lines, EB3 and P3J, were inoculated with herpes simplex virus; EB3 cells were infected at input multiplicities of 15 PFU/cell, and P3J cells were infected at input multiplicities of 10 PFU/cell. The first new virus was seen in P3J cells 15 hr after infection, and peak virus production ($6.5 \log_{10}$ TCID₅₀/ml) occurred at 25-30 hr. The number of viable cells in the infected P3J cells declined markedly and was too low for accurate measurement by 48 hr postinfection. Immunofluorescence staining of infected P3J cells with anti-herpes simplex virus antisera resulted in 80% of the cells showing antigen by 72 hr postinfection. Throughout the course of the experiment, about 2% of P3J cells contained Epstein-Barr virus. Herpes simplex virus replicated much less effectively in EB3 cells than in P3J cells; maximum titers ($4 \log_{10}$ TCID₅₀/ml) were not reached until 240 hr postinfection, and at no time did titers of virus increase appreciably from the initial titer. Viable cells in infected EB3 cultures did not decline markedly, as they did in P3J cultures. Immunofluorescence tests showed that few EB3 cells contained herpes simplex virus antigen. Epstein-Barr virus was found in EB3 cells, but herpes simplex virus did not cause an increase in Epstein-Barr virus titers in EB3 cells. Epstein-Barr virus was apparently not present in cells infected with herpes simplex.

- 1924 HERPESVIRUS TYPE 2 AND CERVICAL CARCINOMA. (E.) Melnick, J. L. (Baylor Coll. Med., Houston, Tex.) and W. E. Rawls. *Ann NY Acad Sci* 174(2): 993-998, 1970.

The presence of antibodies to herpesvirus type 2 was compared in women in various stages of cervical carcinoma in Houston. Eighty-two percent of women from lower socioeconomic levels with cervical carcinoma had antibodies to the virus, while only 22% without cervical abnormalities (controls) had antibodies; 9% of women from higher socioeconomic levels without abnormalities and 31% of those with cervical carcinoma had antibodies to herpesvirus type 2. Seventy-nine percent of women with cervical carcinoma whose lesions consisted of cells containing keratin and large extracellular pearl-like formations of keratin had viral antibodies. Eighty-seven percent of women with lesions with large-cell nonkeratinizing cells had viral antibodies. In women of the lower socioeconomic class, occurrence of antibodies associated with carcinoma *in situ* and cervical dysplasia was not significantly higher than in control women, 26% of cervical dysplasia cases and 38% of carcinoma *in situ* cases, resp., having virus antibodies. Although the cases and controls were not matched for sexual experience, a group of prostitutes was examined in which 54% of the members had antibodies to herpesvirus type 2. Incidence of virus antibody increased with age among women 20-50-yr-old, and declined thereafter.

- 1925 A HUMAN LEUKOCYTE CULTURE WITH AN UNUSUAL CYTOPLASMIC ENVELOPMENT OF HERPES-TYPE PARTICLES. (E.) Chandra, S. (John L. Smith Mem. Inst. Cancer Res., Pfizer Inc., Maywood, N. J.), W. Korol, R. P. Ames, D. P. A. Fabrizio and E. M. Jensen. *Cancer Res* 31(4):441-447, 1971.

Leukocyte cultures prepared from peripheral blood of a 33-yr-old X-ray technician who died of chronic myelogenous leukemia were observed by time-lapse cinematography and it was found that about 70% of the cells exhibited surface activity. The modal chromosome number in the blood cells was 45; there was monosomy in 1 chromosome in group C, and 1 lost G chromosome. The cytoplasm of infected G6 cells contained "naked" herpesvirus particles and virus particles enclosed in membranous sacs. Membranous sacs sometimes enclosed 2-3 particles. The sacs had a distinctive morphology, smooth on their outer surface and fringed on their inner surface. The enveloped herpes virus seen in the cytoplasm of the blood cells may have been a newly synthesized virion in the process of maturation or a reabsorbed virion in the process of degradation.

- 1926 EFFECTS OF CELL FUSION ON PRODUCTION OF THE MOUSE MAMMARY TUMOR VIRUS: IMMUNOFLOUORESCENCE STUDY. (E.) Lasfargues, E. Y. (Inst. Med. Res. Camden, N. J.), B. Kramarsky and D. H. Moore. *Proc Soc Exp Biol Med* 136(3):777-781, 1971.

Fusion of a cell line derived from a spontaneous mammary tumor in a (C57BL x Af) F₁ hybrid mouse with two normal mammary cells lines, MG4 and RMG was induced with Sendai virus; 10 days later the mixed cell cultures and their controls were independently injected s.c. into newborn Amsterdam/IMR rats. Cells containing 2-5 nuclei were readily observed 1 day after fusion and were easily distinguished from the associated MG4 or RMG cells. Within 48 hr about 20% of the cells in the mammary tumor line MG4 population were multinucleated, with 7% being recognized as true heterokaryons. In the mammary tumor line RMG combination a total of 35% were multinucleated cells, with the ratio of heterokaryons roughly 1:3. After 10 days of cultivation nuclear enlargement, multilobulation, nuclear pulverization and chromatin fragmentation were noted in both fused cell populations; these features were rare in the neoplastic cell line and absent in normal cell lines. In the neoplastic line, fluorescein-labeling revealed 10-25% positive cells over a 1-yr period; neoplastic-MG4 fused cells revealed 63, 75, and 84% positive cells in 3 separate experiments in contrast to fusion with RMG rat-mammary cells which gave a ratio of 15, 18, and 28% positive cells. These results were confirmed by whole-cell mount electron microscopy. The findings indicated a significant increase of mammary tumor virus production when neoplastic cells were fused with normal mammary cells from the same species.

- 1927 STUDIES ON ANTIGENIC CROSS-REACTIVITY OF ONCOGENIC RNA VIRUSES: CROSS-REACTIONS BETWEEN MOUSE MAMMARY TUMOR VIRUSES FROM DIFFERENT MOUSE STRAINS. (E.) Blair, P. B. (Cancer Res. Genet. Lab., U. California, Berkeley), D. W. Weiss and G. H. Smith. *Israel J Med Sci* 6(5):611-616, 1970.

Cross-reacting antigenicity between C3H/RIII and DBA strains of mammary tumor virus (MTV) and virus isolated from wild mice has been studied in infected mice from strains DBA, BALB/cfC3H, C3H and RIII. Test mice inoculated with either virus preparation combined with antisera against C3H, CeHf, or C3H/2 tissue did not develop mammary tumors within the test period compared to 3 of 12 females inoculated with RIII virus alone and 5 of 14 females inoculated with RIII virus combined with antiserum against virus-free BALB/c tissue which developed tumors. Antisera from rabbits immunized with the virus-free BALB/c, C57Bl, or I tissue extracts did not neutralize the biologic activity of mammary tumor virus, while antisera from those animals immunized with virus obtained from BALB/cfC3H, BALB/cfDBA, BALB/cfRIII or BALB/cfWILD mice either completely or partially inactivated the biologic activity of the various MTV with only 3 of the 15 test animals developing nodules. In view of the many similarities between mammary tumor virus and various other oncogenic RNA viruses, additional type-specific antigens may be present in the virion coat of the MTV.

- 1928 INTERFERENCE OF GROSS AND BITTNER VIRUSES. THE ANTAGONISM OF THEIR PATHOGENIC ACTION. (Sp.) De Asua, F. J. (Gallego Ctr. Buenos Aires, Argentina) and C. Abaurrea. *Sangre* 15(4):426-434, 1970.

The offspring of a strain of mice with a high incidence of leukemia development were foster-nursed by female mice of a strain having Bittner virus in their mammary milk. The latency period for leukemia development was increased in these foster-nursed mice, and the incidence rate for leukemia declined. Offspring of foster-nursed mice which were nursed by their natural mothers showed the same developments. Mice which developed leukemia in either generation did not develop mammary tumors and mice which developed mammary tumors did not develop leukemia. The reciprocal exclusion of mammary tumor and leukemia may have been due to interference between the pathogenic actions of Gross leukemia virus and Bittner virus, although both can exist together in the same animal. Mother mice dying of leukemia did transmit latent Bittner virus to their offspring, some of which developed mammary tumors, while mothers dying of mammary tumors could transmit leukemia to their offspring.

- 1929 NEUTRALIZATION OF MURINE MAMMARY TUMOUR VIRUS BY SERA OF WOMEN WITH BREAST CANCER. (E.) Charney, J. (Inst. Med. Res., Camden, N. J.) and D. H. Moore. *Nature* 229(5287):627-628, 1971.

Neutralization tests were carried out to determine whether murine mammary tumor virus (MTV) could be neutralized by serum prepared from breast cancer patients. In experiments with human serum, sera were used practically undiluted, and MTV was used in concentration of about 100 ID₅₀/0.1 ml. Inoculation of MTV treated with human breast cancer sera resulted in a mean incidence of MTV infection in C57BL mice of 69% compared to an 87% incidence of infection in mice inoculated with MTV treated with a control serum prepared

from normal human subjects. The presence of neutralizing antibodies in sera from human breast cancer patients and their absence from normal human sera indicated a viral etiology for the human disease.

80 COMPARATIVE PATHOLOGY AND ULTRASTRUCTURE OF RODENT SARCOMAS INDUCED BY THE MURINE SARCOMA VIRUS (MOLONEY). (E.) Perk. K. (Dept. Anim. Nat. Physiol., Hebrew U. Rehovot, Israel) and I. J. *J Comp Path* 81(2):173-178, 1971.

Swiss mice (BALB/c), rats and hamsters were given inoculations of murine sarcoma virus Moloney strain (SV-M), from the first passage to passages as advanced as number 96. In all groups, tumor incidence following virus inoculation was 100%; with successive serial passages a decreasing survival time in inoculated animals was always found. Sarcomas induced in mice by virus from early passage generations were composed primarily of large elongated cells with some port small fibrosarcoma cells and some mononuclear and cells. Tumors were rhabdomyosarcomas, with eosinophilic cytoplasm. Sarcomas induced by virus from later passage generations were composed of undifferentiated spindle cells; these tumors contained a great number of collagen fibers and showed infiltration by mononuclear round cells and leukocytes. These tumors were pleomorphic consisting of large undifferentiated spindle, round, or polygonal cells. Metastatic nodules in lungs were common. Occasionally typical Z bands were evident in tumor cells obtained from animals inoculated with early passage virus. Hamster tumors induced by early passage virus were characteristic spindle-cell sarcomas, and few multinucleated giant cells were also present. Tumors induced by virus passaged 5 times consisted only of round and irregularly shaped cells; multinucleated giant cells were not seen in these tumors. In general, mouse tumors were the most differentiated, and hamster tumors the least differentiated.

81 INFECTION OF MAMMALIAN UNFERTILIZED AND FERTILIZED OVA WITH ONCOGENIC VIRUSES. (E.) Baranska, W. (Wistar Inst. Anat. Biol., Philadelphia, Pa.), W. Sawicki and H. Koprowski. *Nature* 230(5296):591-592, 1971.

The effects of the Rh 911 strain of SV40 Moloney sarcoma virus and SV40 DNA on unfertilized and fertilized ova from 8-10 wk Swiss or C57B1/6 virgin mice were studied. The exposure of unfertilized ova to infection with the 2 viruses had little deleterious effect with some "fragmentation" occurring within 24 hours of cultivation *in vitro*. Similar results were obtained with fertilized ova and most of the ova, fertilized and unfertilized, yielded infectious virus.

82 THE AGE RELATED RESPONSES OF NEW ZEALAND MICE TO A MURINE SARCOMA VIRUS. (E.) Zdzar, A. F. (Natl. Cancer Inst., Natl. Inst. Health., Bethesda, Md.) W. Bietzel and N. Talal. *Int J Exp Immun* 8(3):501-509, 1971.

Murine sarcoma virus (Moloney) was injected s.c. and i.m. into mice of various ages of the following 8 strains: NZB, B/W, NIH Swiss, C57B1/6, C3H, AL/N, DBA/2 and BALB/c. All strains except C3H developed large tumors within 4-5 days after virus injection when virus was injected at 21 days of age or earlier; C3H mice developed smaller tumors than did the other strains, and had a longer latent period. In suckling and weanling mice, 100% of NZB and B/W mice and 93% of NIH Swiss mice had regressed tumors by day 12 postinoculation, while mice of the other 5 strains did not achieve 100% tumor regression until day 21 or later. NZB, B/W and NIH Swiss mice showed shorter periods elapsing between inoculation and the day on which 50% of inoculated mice survived than mice of other strains. An inverse relationship was found between regression time for tumors and age at inoculation; only 4 of 11 NZB mice inoculated at the age of 9 days survived, while 8 of 8 NZB mice inoculated at age 12 days survived. BALB/c mice developed the ability to regress tumors later than other strains. Six-wk-old NZB mice had lower mean tumor regression times than did 8- and 11-month-old mice of this strain.

1933 POTENTIATION OF MURINE SARCOMA VIRUS (HARVEY) (MOLONEY) ONCOGENICITY IN LACTIC DEHYDROGENASE-ELEVATING VIRUS-INFECTED MICE. (E.) Turner, W. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), P. S. Ebert, R. Bassin, G. Spahn and M. A. Chirigos. *Proc Soc Exp Biol Med* 136(4): 1314-1318, 1971.

Adult male BALB/c mice were inoculated with lactic dehydrogenase-elevating virus (LDV) prior to infection with Moloney or Harvey murine sarcoma viruses. LDV-infected mice challenged with Moloney virus developed regressing tumors in 49% fewer cases than Moloney virus-infected mice not previously infected with LDV (controls); LDV-infected mice had a survival time 61 days shorter than the survival time of controls and showed a 75% increase over controls in tumor incidence when challenged with Harvey virus with a complete absence of regressing tumors, compared to 100% tumor regression observed in controls. LDV-infected and Harvey-virus-challenged mice showed a 50% increase in mortality from virus-induced tumors over controls and a 22-day reduction in mean survival time. Inoculation of mice with a 10% extract of tumors from mice dually infected with LDV and Harvey virus produced a 10% tumor incidence in recipients, while LDV-infected mice inoculated with the same preparation showed a 60% incidence of tumor development.

1934 PHYSICAL ALTERATIONS OF A MURINE LEUKEMIA VIRUS COMPLEX IN MAMMALIAN CELL CULTURES. (E.) O'Connor, T. E. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and P. J. Fischinger. *Bibl Haemat* 36:250-256, 1970.

Cat cells were infected with feline leukemia virus (FeLV) and defective murine sarcoma virus; progeny

virus from infected cat cells was described as a FeLV pseudotype of murine sarcoma virus and was thought to consist of a defective murine sarcoma virus genome wrapped in a FeLV virus envelope. This modified murine sarcoma virus readily infected cat cells but not mouse cells; the infectivity of the modified virus for mouse cells could be restored by centrifuging the virus with excess murine sarcoma virus. Dog cell cultures could be infected with modified murine sarcoma virus, as could cultures of human embryonic lung cells. When cells from a cytogenetically abnormal (45 chromosomes) human fetus were infected with modified virus, it was found that the propagation of virus by infected cells decreased as the density of cell plating increased. Normal human embryonic muscle and skin cells and cells from a patient with Down's syndrome were all susceptible to infection with the modified murine sarcoma virus and all gave substantial yields of progeny virus. In all instances, the focus titration pattern of the virus was completely defective, but was normalized by the addition of FeLV during assay.

- 1935 ASPECTS OF THE HARVEY MURINE SARCOMA VIRUS COMPLEX (E.) Harvey, J. J. (Nat'l. Inst. Med. Res., London, England). *Bibl Haemat* 36:240-245, 1970.

A virus of the Harvey murine sarcoma virus family isolated by end-point dilution of Friend virus and designated small spleen virus (SSV) caused only slight splenomegaly in mice when injected alone and markedly reduced the immune response of mice to sheep erythrocytes. In adult BALB/c mice, SSV significantly accelerated erythroblastic splenomegaly caused by Harvey murine sarcoma virus. Sarcomas could not be induced in 3-wk-old BALB/c mice by injection of Harvey virus alone or after preinjection with SSV. However, injection of Harvey virus following SSV produced spleen wt increases more than twice as great as when Harvey virus alone was injected and more than 4 times as great as when SSV alone was injected. Mice given both viruses died within 3 wk with erythroblastic splenomegaly and cystic hemorrhagic lesions in the brain and lungs, while mice given either virus alone survived. SSV apparently enhances the effects of Harvey virus by means of a "helper" function in the Harvey murine sarcoma virus system. It was also reported that virus particles of an unusual "spoked" morphology were found in hamster sarcoma cells transformed by Harvey and Moloney murine sarcoma viruses.

- 1936 PROPERTIES OF A MURINE SARCOMA VIRUS. (E.) Kirsten, W. H. (Dept. Path., U. Chicago, Ill.), V. Schauf and J. McCoy. *Bibl Haemat* 36:246-249, 1970.

The comparative defectiveness of murine sarcoma virus Moloney strain (MSV-M) and murine sarcoma virus strain K (MSV-K) was investigated by observing early titers of these viruses in infected 3T3 mouse cells. The latter virus which was first recovered from high-titer pools of rat-adapted murine erythroblastosis virus was obtained in the present experiment from

mouse sarcomas, rat erythroblastosis virus and supernatants of murine sarcoma virus-transformed cells. Early (2 days postinfection) harvests of MSV-K virus derived from mouse sarcomas and rat erythroblastosis cultures yielded titration patterns which were independent of virus dilution in the cell cultures, while titers of virus from transformed mouse cells could be increased by the addition to the cultures of murine erythroblastosis virus. MSV-M virus titers could also be increased by addition of murine erythroblastosis virus, suggesting that this virus and MSV from transformed 3T3 cells were defective.

- 1937 TRANSFORMATION OF A CLONED RENAL EPITHELIAL CELL LINE BY MOLONEY MURINE SARCOMA VIRUS (M-MSV). (E.) Ikawa, Y. (Nat'l. Inst. Hlth., Tokyo, Japan), H. Yoshikura and H. Sugano. *Bibl Haemat* 36:312-322, 1970.

A clone of epithelial cells prepared from the kidney of mice and designated C3H2KB was infected with Moloney murine sarcoma virus (M-MSV) at varying dilutions and prepared for microscopic examination. Infected monolayers showed loose transformed foci consisting of refractile cells by day 4 postinfection. The number of foci was proportional to the titer of the M-MSV preparation used to infect the cells, showing a 1-hit dose response with 10^{-1} virus dilutions and a 2-hit dose response with 10^{-3} dilutions. Some foci were made up of small piles of spindle-cells and some were made up of small round cells; both types of cells in foci showed budding virus. M-MSV-transformed cells were implanted s.c. on the backs of male C3H/He mice; 12 of 20 mice receiving transplants developed local dorsal anaplastic medullary carcinomas which contained virus particles. When transformed cells were subcultured, they came to resemble normal C3H2KB cells after 8 subcultures.

- 1938 NEOPLASTIC BONE LESIONS INDUCED IN RATS AND HAMSTERS BY MOLONEY AND HARVEY MURINE SARCOMA VIRUSES. (E.) Soehner, R. L. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston), S. Fujinaga and L. Dmochowski. *Bibl Haemat* 36:593-599, 1970.

Newborn rats and hamsters were inoculated i.p. with 0.2 ml of supernatants of homogenates of tumors induced by Harvey or Moloney strain murine sarcoma viruses. Both viruses induced bone tumors in rats; Moloney virus proved to be the more feasible experimental system, however, for Harvey virus usually killed rats before tumors had a chance to develop in the extremities. Moloney virus caused bone tumors in 1 of 9 injected rats with a 45 day latency; serially passaged virus caused incidences of bone tumors in rats ranging from 50-100%, with latencies ranging from 13-28 days. Harvey virus also caused bone tumors in hamsters; however, serial passage did not increase the tumor incidence among hamsters. Serial passage of Moloney virus-induced bone tumors increased the incidence of tumors in hamsters and shortened the latent period for tumor appearance.

-type virus particles were found in rat and hamster
one tumors induced by both Moloney and Harvey virus
strains.

939 EFFECT OF GROWTH ON THE GLYCOPROTEINS
FROM THE SURFACE OF CONTROL AND ROUS SAR-
COMA VIRUS TRANSFORMED HAMSTER CELLS. (E.) Buck,
A. (Div. Biol. Kansas St. U., Manhattan), M. C.
lick and L. Warren. *Biochemistry* 10(11):2176-2180,
1971.

aby hamster kidney cells in the plateau growth
phase and in the logarithmic growth phase were grown
in the presence of ^{14}C -labeled L-fucose-1 or L-fucose-2,
harvested, digested with pronase and subjected to gel
filtration tests. The material from rapidly growing
cells enriched with cell surface glycopeptides eluted
early from the column; material from slowly growing
cells had a comparatively small proportion of rapid-
ly migrating glycopeptides. The relative amounts of
early-eluting glycopeptides was also more abundant
for Rous sarcoma virus-transformed cells and de-
creased as the cells entered the slow plateau phase
of growth. However, material from virus-transformed
cells was more enriched with early-eluting glycopep-
tides than was material from untransformed cells.

940 THE RNA OF RNA-CONTAINING TUMOR VIRUSES.
(E.) Bader, J. P. (Natl. Cancer Inst.,
Natl. Inst. Hlth., Bethesda, Md.). *Bibl Haemat*
5:140-143, 1970.

the interval between completion of synthesis of viral
RNA by Rous-associated virus and Rauscher murine
leukemia virus was investigated by exposing infected
cells to ^3H -uridine and collecting fluids at 10 or
5 min intervals. Radioactive virion RNA was first
detected 80 min after the addition of labeled uridine,
indicating that the minimum interval between com-
pletion of viral RNA synthesis and its incorporation
into virions is about 70-75 min. RNA produced by
these viruses was found to be conventional viral RNA;
no labeled cellular RNA was found. When actinomycin
(2 $\mu\text{g}/\text{ml}$) was added to cultures of virus-infected
cells within 15 min after the addition of ^3H -uridine
to the cultures, the appearance of labeled RNA was
prevented; addition of actinomycin D 30 min after
uridine did not affect the appearance of labeled RNA.
Cycloheximide (10 $\mu\text{g}/\text{ml}$) addition resulted in inhibi-
tion similar to that produced by actinomycin D.

941 DEOXYRIBONUCLEIC ACID POLYMERASES OF ROUS
SARCOMA VIRUS: KINETICS OF DEOXYRIBONUCLEIC
ACID SYNTHESIS AND SPECIFICITY OF THE PRODUCTS. (E.)
Garapin, A. C. (Dept. Microbiol., U. California, San
Francisco), L. Fanshler, J. A. Leong, J. Jackson, W.
Levinson and J. M. Bishop. *J Virol* 7(2):227-232, 1971.

the interrelationship between the synthesis of single-
stranded DNA in association with the RNA genome of
the virus and the synthesis of double-stranded DNA
by an enzyme capable of utilizing double-stranded DNA
as a template has been studied in Rous sarcoma virus

by analyzing the kinetics of DNA synthesis at limiting
substrate concentrations. At very low substrate con-
centrations (thymidine triphosphate was limited) the
initial enzymatic product was single-stranded DNA,
both free and complexed to viral RNA, and after an
appreciable time the final double-stranded DNA was
detected. At higher concentrations the final double-
stranded DNA was detected much earlier in the reaction.
Both products contained nucleotide sequences which
were complementary to regions in the 70S viral RNA;
with hybridization only a small amount of DNA annealed
to any given RNA molecule to give hybrids having a
buoyant density virtually identical to that of single-
stranded RNA. The results suggest that segments of
the 70S viral RNA are transcribed into single-stranded
DNA followed by synthesis of double-stranded DNA which
utilizes the primary enzymatic product as template in
a manner not yet determined.

1942 NUCLEOTIDE COMPOSITION OF RNA HYBRIDIZED
TO HOMOLOGOUS DNA FROM CELLS TRANSFORMED
BY AVIAN TUMOUR VIRUSES. (E.) Baluda, M. A. (UCLA
Sch. Med., Los Angeles, Calif.) and P. D. Markham.
Nature 231(20):90-91, 1971.

The average base composition of the RNA which was
hybridized to homologous DNA from chick embryo fibro-
blasts transformed by Schmidt-Ruppin Rous sarcoma
virus (SR-RSV) or avian myeloblastosis virus (AMV)
was compared with the base composition of the input
viral RNA. The use of fragmented viral RNA and a
modified washing procedure which excluded the use
of ribonuclease assured the recovery of all the ribo-
nucleotides which had been hybridized and the absence
of partially hybridized ribonucleotide sequences.
The base compositions of hybridized ^{32}P -RNA and of
input ^{32}P -SR-RSV-RNA were identical; similar results
were found for ^{32}P -AMV-RNA. These results provide
further evidence for a DNA intermediate in the re-
plication of RNA tumor viruses.

1943 DEOXYRIBONUCLEIC ACID POLYMERASE ASSO-
CIATED WITH AVIAN TUMOR VIRUSES: SECON-
DARY STRUCTURE OF THE DEOXYRIBONUCLEIC ACID PROD-
UCT. (E.) Fanshler, L. (Dept. Microbiol., U.
California, San Francisco), A. C. Garapin,
J. McDonnell, A. Faras, W. Levinson and J. M.
Bishop. *J Virol* 7(1):77-86, 1971.

The major product of DNA synthesis by the Rous
sarcoma virus-associated polymerase was a DNA:RNA
hybrid which co-sedimented with 70S viral RNA and
had the same buoyant density as that of single-
stranded RNA. This 70S DNA:RNA eluted from hydrox-
yapatite in a manner similar to that of isolated
70S viral RNA. Treatment of the 70S complex with
ribonuclease in 0.3 M NaCl gave a 4S DNA:RNA hybrid
with approximately equimolar DNA and RNA contents
and which eluted from hydroxyapatite similarly to
single-stranded RNA. The late product contained
DNA which was not associated with RNA; analysis
by hydroxyapatite chromatography indicated that
the late product had little single-stranded DNA
but seemed to consist of double-stranded DNA. By

12 hr after initiation of enzymatic synthesis, no hybrid molecules were detectable in the product, which consisted primarily of double-stranded DNA.

- 1944 INHIBITION OF GROWTH OF UNINFECTED AND ROUS SARCOMA VIRUS-INFECTED CHICK-EMBRYO FIBROBLASTS BY RIFAMPICIN. (E.) Robinson, H. L. (Stanford U. Sch. Med., Calif.) and W. S. Robinson. *J Nat Cancer Inst* 46(4):785-788, 1971.

The effect of rifampicin on the growth of uninfected and Rous sarcoma virus-infected chick embryo fibroblasts was studied in 10-day chick embryo cultures by means of virus infectivity assay and cell counting techniques. Cells not treated with rifampicin proliferated with a doubling time of around 20 hrs whereas concentrations as low as 20 µg/ml inhibited the growth of both normal and transformed cells, the degree of inhibition correlating with the concentration of the drug and the length of time of exposure. The agent had little or no effect on virus production by cultures grown in the presence of the drug for 24 or 48 hrs but at 72 and 96 hrs the amount of virus produced was markedly decreased in response to 60 µg/ml of the agent. These results suggest that the inhibition of focus formation may be due to inhibition of cell growth rather than to a specific effect of the drug on cell transformation.

- 1945 LACK OF CORRELATION BETWEEN CONVERSION BY RNA TUMOUR VIRUSES AND INCREASED AGGLUTINABILITY OF CELLS BY CONCANAVALIN A AND WHEAT GERM AGGLUTININ. (E.) Moore, E. G. (McArdle Lab. Cancer Res., U. Wisconsin, Madison) and H. M. Temin. *Nature* 231(5298):117-118, 1971.

Agglutination studies with wheat germ agglutinin and concanavalin A of parallel uninfected, and Rous sarcoma virus (RSV)-and avian leukosis virus (RAV)-infected chicken cells, and parallel uninfected and murine sarcoma virus (MSV)-and murine leukemia virus (MLV)-infected rat and mouse cells, all in secondary or tertiary cultures, were performed. A serological scale of 0 to +++, based primarily on the cell aggregate size was used to estimate the degree of agglutination, and the specificity of the agglutinin cell interaction was demonstrated. In agreement with earlier findings, normal cells showed negligible or very low agglutinability. Significant increases were found after trypsin treatment. With the exception of B77-virus-converted rat cells, cells converted by these RNA tumor viruses (Schmidt-Ruppin virus, B77 virus, P-RSV, MSV) did not show marked increases in agglutinability. Rat cells converted by B77 virus, however, displayed markedly increased agglutinability. Control experiments were able to confirm the increased agglutinability of mouse cells transformed by DNA tumor viruses. These results demonstrate that changes in response to wheat germ agglutinin and concanavalin A are not necessary concomitants of neoplastic transformation in cell culture.

- 1946 ULTRAVIOLET SPECTROGRAMMIC MICROSCOPE STUDIES OF ROUS SARCOMA VIRUS CULTURED IN CELL-FREE MEDIUM. (E.) Alexander-Jackson, E. (U. San Diego, Calif.). *Ann NY Acad Sci* 174(2):765-781, 1970.

Partially purified Rous sarcoma virus was filtered into cell-free broth and examined under the UV spectrographic microscope. After 8 hr of incubation in the broth, spectrograms revealed marked molecular activity, including an increase in DNA; DNA had decreased by 16 hr of incubation. Under the electron microscope, virus-containing filtrates showed the presence of small zooglycal symplasm L forms, and a few small coccid bodies. Pleomorphic L forms similar to mycoplasma and some slender filaments were seen after 8 hr in culture. By 16 hr, many acid-fast and nonacid-fast bodies were seen. Filtered growth broth streaked on agar did not grow although unfiltered broth which contained virus did show growth on agar; the growth resembled the bacterial isolates sometimes seen in association with Rous sarcoma virus infection.

- 1947 A DEFECTIVE ROUS SARCOMA VIRUS: THE D-5 STRAIN. (Rus.) Kuznetsov, O. K. (N. N. Petrov Res. Inst. Oncol., Leningrad, U.S.S.R.) and A. M. Dyad'kova. *Vop Onkol* 17(1):35-41, 1971.

The D-5 strain of the Rous sarcoma virus (RSV) isolated from chicken tumor cells and purified of its contaminant Rous leukosis virus (CRV₅) was capable of inducing transformation foci in normal chicken embryo cell cultures. The transformed cells constituted 3 categories: non-virus producing, low yield virus-producing or high yield virus-producing cells. Superinfection of these transformed cell cultures with avian leukosis virus, RAV-1, or with the CRV₅ strain led to the production of RSV particles by former non-virus producing cells and increased the yield in RSV particles in low-yield virus-producing cells. The D-5 strain was thus considered to be a defective strain and named D-5(0); the leukosis viruses (including the CRV₅) were considered to be helper viruses because of their capacity to activate the reproduction of the D-5(0) virus. The defective virus exhibited no interference with the avian leukosis viruses of subgroups A or B and gave no cross-reactions of neutralization with viruses of subgroups A, B or C. When contaminated with the CRV₅-strain of subgroup A, the virus exhibited features of an RSV of subgroup A in the interference and neutralization reactions. The D-5(0) virus could not be classified under any of the subgroups A, B or C by its immunological behavior in the absence of its contaminant.

- 1948 CHANGES AT THE MEMBRANES OF LEUKOSIS VIRUS TRANSFORMED CELLS AND VIRUS AS DETECTED BY ELECTRONMICROSCOPY. (E.) Morgan, H. R. (U. Rochester Sch. Med. Dent., N. Y.). *Bibl Haemat* 36:144-147, 1970.

nicked embryo fibroblasts were infected with Fujinami strain Rous sarcoma virus and treated with hyaluronidase (300 National Formulary U) in order to remove the layer of acid mucopolysaccharide covering the surface of infected cells. Under the electron microscope, large masses of virus particles could be seen on the surfaces of infected cells not treated with hyaluronidase, and the masses were covered with a layer of acid mucopolysaccharide. Some virus particles incorporated the acid mucopolysaccharide lay into the viral envelope as they budded from transformed cells. No virus particles were seen in cultures treated with hyaluronidase, suggesting that the enzyme had released the viral aggregates from the cell surface.

49 FAILURE TO DETECT HOMOLOGY BETWEEN THE DNA OF THE SHOPE FIBROMA VIRUS AND THE DNA OF A HYPERSENSITIVE CELL. (E.) Jacquemont, B. (Natl. Inst. Med. Res., Lyon, France), M. H. Richard and J. Grange. *J Gen Virol* 10(3):237-242, 1971.

The structural homology between the DNA of Shope fibroma virus and that of RK 13 cells of a DNA-DNA hybridization were studied in infected RK 13 cell cultures and tumors of adult rabbits by thymidine labeling. Shope fibroma virus DNA hybridized more than 70% with its homologue; the percentage hybridization obtained with the DNA of RK 13 cells of calf thymus and *E. coli* were similar to those obtained with the background. A constant quantity of labeled DNA from RK 13 cells showed hybridization with its homologue (30%), with calf thymus DNA (6.4%), with DNA from *E. coli* (2.2%) and with Shope fibroma virus DNA (1.2%). Absence of hybridization between the Shope fibroma virus DNA and DNA of the rabbit cell could mean that there is a difference between the mechanism of induction of tumors of Shope fibroma virus and other oncogenic viruses.

50 TRANSFER RNA METHYLASES OF NORMAL CELLS, VIRUS-TRANSFORMED CELLS AND TUMORS DERIVED FROM TRANSFORMED CELLS. (E.) Fujioka, S. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), R. C. Ting and R. C. Gallo. *Cancer Res* 31(4):1445-1456, 1971.

tRNA methylase (tRNA methylase) was assayed in normal Swiss or C3H mouse embryo cells, normal rat kidney cells, rat kidney cells transformed by SV40, polyoma virus or murine sarcoma virus Moloney, and in tumors obtained by inoculating rats with murine sarcoma virus-transformed cells. No differences were observed between tRNA methylase specific activity or capacity in normal cells and murine sarcoma virus-transformed cells; the tRNA methylase capacity of normal cells and of transformed cells was 59.1 and 59.0 pmoles of S-adenosyl-methionine/ μ g of tRNA, resp. Specific tRNA methylase activities in normal and murine sarcoma virus-transformed cells were 24.0 and 26.2 pmoles of S-adenosyl-methionine/25 μ g of tRNA, resp. Both specific activity and capacity were increased 2-6-fold in tumors induced by murine sarcoma virus-transformed

cells over specific activity and capacity in normal tissues. SV40 and polyoma virus-transformed cells contain higher tRNA methylase activities and capacities than nontransformed normal cells. tRNA methylase capacity in normal and polyoma virus-transformed cells was 33.8 and 53.2 pmoles of S-adenosyl-methionine/ μ g of tRNA, resp.; tRNA specific activity in normal and SV40-transformed cells was 16.3 and 36.9 pmoles of S-adenosyl-methionine/25 μ g of tRNA, resp.

1951 INFECTIVITY OF MOLECULAR FORMS OF SIMIAN VIRUS 40 DNA. (E.) Trkula, D. (Baylor Coll. Med., Houston, Tex.), S. Kit, T. Kurimura and K. Nakajima. *J Gen Virol* 10(3):221-229, 1971.

The infectivities of superhelical simian virus 40 (SV40) DNA extracted from African green monkey kidney cells with the products formed when purified SV40 DNA was adsorbed to replicate monolayer cultures of African green monkey kidney cells, transformed human skin and primary mouse kidney cells for various periods of time was studied by means of thymidine labeling techniques. Approximately 23-48% of the input viral 3 H-DNA was adsorbed to African green monkey kidney cells, human skin cells and mouse kidney cells in 2 hr. Approximately 1/3 of the denser Form I DNA was converted to less dense, nicked DNA during the 2 hr adsorption period to African green monkey kidney cells, 40% with transformed human skin cells and about 25% with mouse kidney cells. Specific infectivities of DNA extracted from the cultures were of the same magnitude as that of input DNA in the 3 types despite the fact that as much as 69% of the extracted DNA represented nicked molecular forms. At 37-39 hr after infection, about 76% of the radioactivity was recovered in the heavy DNA peak and about 21% in the light DNA peak from SV40-infected African green monkey kidney cells, with the heavy fractions showing a sedimentation coefficient of about 21S (Form I DNA) and 16-18S; the latter showed 25% of the specific infectivity of Form I DNA.

1952 RELATIONSHIP BETWEEN VIRUS-INDUCED CELLULAR DEOXYRIBONUCLEIC ACID SYNTHESIS AND TRANSFORMATION BY SIMIAN VIRUS 40. (E.) Fox, T. O. (Dept. Biochem., Princeton U., N. J.) and A. J. Levine. *J Virol* 7(4):473-477, 1971.

Monolayer cultures of 3T3 mouse cells labeled with 32 P were infected with simian virus 40 (SV40); 2 hr later 3 H-thymidine was added and at 24 hr and 48 hr after infection the infected cells were sedimented through a Ficoll gradient. Transformation frequencies of cells obtained 24 hr after infection with a fast sedimenting peak (in the S period) were 40-57% compared to 7-12% for cells with a slow sedimenting peak (in the G-1 period). After 48 hr the fast sedimenting peak gave transformation values of 9-26% compared to 8-32% for the slow sedimenting peak, resulting in ratios of fast sedimenting transformation to slow sedimenting transformation that were considerably lower for the 48 hr sample than for the 24 hr sample. These results indicated that cellular DNA synthesis during the first 24 hr after infection of 3T3 cells is necessary for efficient transformation.

- 1953 STRUCTURAL PROTEINS OF SIMIAN VIRUS 40.
(E.) Barban, S. (Natl. Inst. Allerg.
Infect. Dis., Natl. Inst. Hlth., Bethesda, Md.)
and R. S. Goor. *J Virol* 7(2):198-203, 1971.

The characteristics of structural proteins of simian virus 40 (SV40) in infected African green monkey kidney cells and Vero cells were analyzed by polyacrylamide gel electrophoresis and isoelectric focusing procedures. Staining patterns showed 2 major bands and 3-4 minor bands; virions labeled with ^3H - or ^{14}C -amino acids gave relative proportions of radioactivity of 80% for peaks I and II, 7% for peak III, 7-9% for peak IV and 4% for a slowly migrating band at the top of the gel with estimated molecular weights of approximately 45,000 (I, II), 29,000 (III), and 16,000 (IV) daltons. The fastest sedimenting peak (I) with 35-40S value was identified as the nucleocapsid-DNA complex; the second major peak (II) had an S value between 2.5-5.0 and was associated with the viral capsid protein, which was separated into 2 components with isoelectric optima of pH 6.4 and 5.5. Immunological analysis of peaks I and II revealed 2 distinct precipitin lines with rabbit antiserum prepared against highly purified dissociated SV40 particles. The location of the peak III peptide in the architecture of the virion is not known.

- 1954 HOMOLOGY BETWEEN SV40 DNA AND DNA OF NORMAL AND SV40-TRANSFORMED CHINESE HAMSTER CELLS.
(E.) Hirai, K. (Wistar Inst. Anat. Biol., Philadelphia, Pa.) and V. Defendi. *Biochem Biophys Res Commun* 42(4): 714-722, 1971.

The extent of the homology between simian virus 40 (SV40) DNA and the DNA of normal and virus-transformed Chinese hamster cell has been studied by DNA-RNA hybridization techniques. The size of the complementary RNA (cRNA) synthesized *in vitro* by *E. Coli* DNA-dependent polymerase was rather heterogeneous, with a peak of 10S and a broad distribution above and below this value. The thermal stability of DNA-RNA complexes indicated that long RNA molecules from both cell lines were involved. The heat stability of SV40 DNA + cell DNA hybrids was different from that of ^3H -SV40 DNA + SV40 DNA hybrids and from ^3H -cell DNA + cell DNA hybrids. Results indicated that normal Chinese hamster DNA as well as SV40-transformed cells do contain some homologous nucleotide sequence comparable to SV-40 DNA.

- 1955 ELECTRON MICROSCOPIC DETECTION OF TRANSFORMING VIRUSES INDUCED BY CELL ASSOCIATION: I. THE SV40 MODEL. (E.) Menezes, J. (Fac. Med. U. Ottawa, Ontario, Canada). *Int J Cancer* 7(2):331-338, 1971.

SV40-transformed cells were co-cultivated or fused with permissive or insusceptible cells from monkey, bovine, porcine or hamster cell cultures; cell fusion was accomplished by mixing, centrifuging and

cultivating the 2 cell types to be fused in the presence of UV-inactivated Sendai virus. Fusion and co-cultivation products were examined under the electron microscope to detect SV40 particles, and detection of virus by electron microscopy was compared with detection of virus by infectivity tests. An average of approximately 2 SV40-infected cells containing virus particles were needed for a positive detection of SV40 particles by microscopy, whereas infectivity tests yielded positive results using fewer cells. The minimum time required to detect SV40 in cell cultures after infection, co-cultivation or fusion was about 1-2 hr less using electron microscopy than it was using infectivity tests. Naturally insusceptible cells could be successfully used for the induction of a virus by fusing these cells with transformed cells.

- 1956 STUDIES ON THE HAMSTER PAPILLOMA AND THE HAMSTER VIRUS LYMPHOMA. (E.) Graffi, A. (German Acad. Sci., Berlin), E. Bender, T. Schramm, I. Graffi and D. Bierwolf. *Bibl Haemat* 36:293-303, 1970.

Papova virus was found in papillomas arising from the hair follicles of young hamsters; although the tumors were readily transplantable, no viruses were found in transplanted papillomas. S.C. inoculation of cell-free virus filtrate from the papillomas into newborn hamsters yielded 5-10% tumor incidence; inoculation with skin tumor preparations also produced a 30-80% incidence of leukemia and lymphoma with latencies of 4-8 wk. Lymphomas often affected the thymus, kidneys and liver. Papova virus DNA whether administered with or without RNase produced high incidences of lymphomas. Antipapova virus antiserum prepared in rabbits counteracted the oncogenic effects of the virus; only 3 of 64 hamsters injected with a virus concentration of 1:10 and immunized with anti-papova virus antiserum developed lymphomas.

- 1957 GLYCOPEPTIDES FROM THE SURFACE OF CONTROL AND VIRUS-TRANSFORMED CELLS. (E.) Buck, C. A. (Div. Biol., Kansas St. U., Manhattan), M. C. Glick and L. Warren. *Science* 172(3979):169-171, 1971

Normal and polyoma virus-transformed hamster cells, normal and murine sarcoma virus-transformed BALB/3T3 mouse cells, and normal and Rous sarcoma virus-transformed chick embryo cells were digested in trypsin to remove glycopeptides. Glycopeptides from normal and transformed cells were digested exhaustively with pronase and prepared for gel filtration (Sephadex G-50). In every case, elution patterns on gel filtration showed glycopeptides from transformed cells eluting 5-10 fraction numbers ahead of glycopeptides from normal cells. Results were similar for all cell of whatever origin, transformed by all the various viruses.

- 1958 GLYCOSYLTRANSFERASE ACTIVITIES IN NORMAL AND POLYOMA-TRANSFORMED BHK CELLS. (E.) Den, H. (Dept. Biol., Johns Hopkins U., Baltimore,

d.), A. M. Schultz, M. Basu and S. Roseman. *J Biol Chem* 246(8):2721-2723, 1971.

Normal and polyoma virus-transformed baby hamster kidney fibroblasts showed differing levels of sialyltransferase activity. The activity of the sialyltransferase catalyzing the formation of hematoside from lactosylceramide and cytidine monophospho-N-acetylneuraminic acid was reduced to about 15% of normal cell levels in virus-transformed cells. Sialyltransferase activity in homogenates from normal cells was markedly increased (about 6-fold) when certain phospholipids were added to the incubation mixtures; phospholipids exhibiting the greatest stimulatory effect were phosphatidylglycerol and cardiolipin. In virus-transformed cells, galactosyltransferase was reduced to 36-49% of normal cell levels, and glucosaminyltransferase was reduced to 87% of normal cell values. Phosphatidylglycerol and cardiolipin had no effect on sialyltransferase in virus-transformed cells that was comparable to their effect on normal cells.

59 FURTHER MANIFESTATIONS OF ABORTIVE TRANSFORMATION OF BHK 21 CELLS BY POLYOMA VIRUS. (E.) Taylor-Papadimitriou, J. (Emp. Cancer Res. Fund Lab., London, England), G. P. Stoker and P. Riddle. *Int J Cancer* (2):269-276, 1971.

The effect of polyoma virus on resting baby hamster kidney 21 cells in serum-deprived cell cultures was studied by means of autoradiography and time-lapse cinematography. Over 50% of the cells were stimulated by virus to incorporate ³H-thymidine over a 48 hr period in the absence of serum; the addition of serum did not markedly affect the percentage of cells stimulated. In contrast, control extracts of mouse embryo cells showed a serum concentration-related response. Approximately 21-60% of the cells infected with partially purified virus incorporated ³H-thymidine, while those exposed to empty capsids did not. Viral-stimulated DNA synthesis first appeared after about 30 hr. Disorientation of infected cells was first detectable after 25-30 hr and was maximal 2-3 days after infection as determined by time-lapse cinematography. It now seems likely that different cells have different requirements for the factors in serum which are required for growth and integrity.

60 TRANSPORT INHIBITORS RELEASED BY 3T3 MOUSE CELLS AND THEIR RELATION TO GROWTH CONTROL. (E.) Pariser, R. J. (Med. Coll. Virginia, Richmond) and D. D. Cunningham. *J Cell Biol* 49(2):525-529, 1971.

Transport of uridine-³H and phosphate-³²P into the acid-soluble fraction of 2 lines of mycoplasma-free confluent cells (3T3 and polyoma-transformed Py3T3) was assayed 20 min after the initiation of cell division by the addition of 10% serum medium. When 3-altered medium with 10% fresh serum was added to confluent cultures, only 65% and 33% transport-

stimulating activity was observed, resp., for phosphate and uridine compared to 100% activity for fresh medium with 10% serum; 3T3-altered, dialyzed medium showed 48% and 60% activities, resp., while 3T3-altered, dialyzed medium with 10% fresh serum showed 90% and 108% activities, resp. The increase in activity of exhaustively dialyzed 3T3-altered medium from which a free inhibitor was presumably lost suggested that the serum possessed transport-stimulating activity other than that due to the simple binding of inhibitor. Subconfluent 3T3 cells were fully able to reduce the transport-stimulating activity of fresh medium at a rate roughly equal to that for confluent 3T3 cells. Noncontact-inhibited (subconfluent and Py3T3) cells released an inhibitor for uridine transport only, and they inactivated stimulatory factors for both uridine and phosphate transport present in fresh 10% serum medium.

1961 TESTS FOR ONCOGENICITY OF VIRUSES UNDER CONDITIONS OF ALTERED HOST AND VIRUS. (E.) Larson, V. M. (Merck Inst. Ther. Res., West Point, Pa.), P. A. Conrad, W. R. Clark and M. R. Hilleman. *Proc Soc Exp Biol Med* 136(4):1304-1313, 1971.

Hamsters were thymectomized at birth and at various times thereafter were inoculated s.c. with viruses of various strains in various multiplicities. Thymectomized hamsters given polyoma virus at 7 days of age developed tumors in 83% of cases, while thymectomized hamsters given polyoma virus at 4 months of age developed tumors in 28% of cases; nonthymectomized hamsters inoculated at 7 days of age developed tumors in 37% of cases and in 7% of cases inoculated at 4 months of age. Tumorigenesis by SV40 was similarly enhanced by thymectomy; 80% of the thymectomized animals and 42% of the sham-operated animals developed tumors. Tumor induction by adenovirus 7 was enhanced by thymectomy (70% of thymectomized and 12% of unthymectomized animals developed tumors), and tumor induction by adenovirus 3 was moderately enhanced by thymectomy. Thymectomized hamsters were also inoculated with influenza virus, poliovirus, ECHO virus, reovirus, vaccinia virus or *Mycoplasma orale*; tumor induction with these agents was rare in both thymectomized and unthymectomized animals. Hamsters given inoculations of adenovirus when newborn, 1-, 3-, or 12.5-14-month-old developed tumors in the newborn group only; however, SV40 induced tumors in animals of all ages. While the tumorigenicity of the viruses depended on the amount of virus inoculated, virus strain and passage level did not appreciably affect the tumorigenicity of the virus used.

1962 TRANSFER RNA METHYLASE ALTERATIONS IN POLYOMA TRANSFORMED RAT EMBRYO CULTURE CELLS (E.) Gallagher, R. E. (Natl. Inst. Hlth., Bethesda, Md.), R. C. Y. Ting and R. C. Gallo. *Proc Soc Exp Biol Med* 136(3):819-823, 1971.

Cells from 12-day-old embryos of inbred BN rats transformed with polyoma virus SE3049 were injected into

adult BN rats; cultures of the resulting tumor were treated with *E. coli* tRNA (30µg) or yeast tRNA (60µg) prior to ¹⁴C- methyl group incorporation determinations. With *E. coli* tRNA as methyl acceptor and with excess amounts of enzymes, label incorporation showed a 3-6-fold difference in rate of reaction, and a 7-fold increment in the extent of methylation was noted in the tumor cell system. With yeast tRNA, methylation was almost undetectable in the nontransformed control cells but reached an extent of approximately 0.7 µmoles/mg of tRNA with the tumor preparation. Uridine-labeled tRNA after 90 min incubation accounted for 92% of the acid precipitable counts in the control system, compared to 61% in the tumor system; the presence of ammonium ions did not affect the rate of reaction. The marked differences in capacity to methylate heterologous tRNA substrates suggests that qualitative differences may exist between the methylases of paired cell lines.

1963 VIRAL SENSITIVITY OF CELLS DERIVED FROM NORMAL OR PATHOLOGICAL RABBIT TISSUE. (F) Chardonnet, Y. (Fac. Med. Lyon, France) and L. Barrilliot. *Path Biol* 19(1-2):65-75, 1971.

See also:

- * (Rev): 1733, 1734, 1735, 1739, 1752, 1755, 1756
- * (Chem): 1836, 1837
- * (Phys): 1838
- * (Immun): 1964, 1965, 1966, 1967, 1968, 1970, 1971, 1972, 1973, 1974, 1975, 1976, 1977, 1978, 1979, 1980, 1981, 1982, 1995

1964 IMMUNOLOGIC REACTIVITY TO VIRAL ANTIGENS IN CHICKENS INFECTED WITH AVIAN LEUKOSIS VIRUSES. (E.) Meyers, P. (Dept. Microbiol., U. Miami, Fla.) and R. M. Dougherty. *J Nat Cancer Inst* 46(4): 701-711, 1971.

The effect of congenitally transmitted avian leukosis virus on the immunologic responsiveness of chickens to related and unrelated viruses was studied utilizing chick-embryo fibroblast tissue cultures by means of hemagglutination-inhibition testing. All congenitally infected birds at ages 2½, 6 and 25 wk retained their viremia for the entire 8 wk of the experimental period and failed to produce antiviral neutralizing antibody with the exception of one bird in the 2½-wk-old group, which developed a low but significant level of antibodies by 8 wk which coexisted with the viremia. In the control group, the youngest age groups had uniform responses in terms of viremia, and antibody production with viremia became apparent by wk 1 and persisted until wk 5. Antibodies to RAV-1 strain of avian leukosis virus first appeared in these groups at 2 wk with higher titers noted at 8 wk. In contrast, viremia and antibody developed in a smaller proportion of the 23-wk-old chickens, the viremia was of shorter duration and ultimate antibody titer was lower. When challenged with heterologous influenza virus A, control and congenitally infected birds in all age groups responded with high titers of antibody, with the congenitally infected 2½-wk-old group showing lower titers by one-half than the appropriate control group. Response to AV-6 Harris strain of avian leukosis virus was similar in 25-wk-old birds of both control and congenitally infected groups, whereas in 6-wk-old birds 18 of 19 control as compared to 6 of 17 congenitally infected birds developed antibodies to the virus. Age-dependent inhibition of RAV-6 antibody response in congenitally infected birds cannot at this time be explained.

1965 EXTRACTABLE HERPESVIRUS ANTIGENS FROM CHICKENS WITH MAREK'S DISEASE. (E.) Ahmed, M. John L. Smith Mem. Cancer Res., Pfizer Inc., Maywood, N.J.), J. B. Leech, S. M. Slattery and G. Schidlovsky. *Int J Cancer* 7(2): 339-345, 1971.

Feather follicles from chickens infected with Marek's disease herpesvirus (MDHV) were prepared by centrifugation and sonication for immunofluorescence and microimmunodiffusion tests. Both tests demonstrated MDHV antigens in epithelial cells from follicular tissue. Positive antigen reactions were also obtained from chickens exposed to Marek's disease virus by direct contact. Marek's disease-free chicken follicular tissues were antigen-negative. Testis, ovaries, liver, spleen, kidney, heart, brain, bursa and bone marrow preparations from Marek's disease-infected chickens did not harbor MDHV antigen. Normal chicken serum and serum containing antibodies to Rous sarcoma virus did not react with the follicular tissue MDHV antigen. Marek's disease antibodies were found in sera from some but not all chickens with and without gross pathology which had been infected with MDHV. Antigens extracted from virus-containing follicular epithelial cells growing *in vivo* or *in vitro* were of a similar nature. Chicken sera positive for Marek's disease antibodies caused specific coating of MDHV particles.

1966 EXPERIENCES WITH COMPLEMENT FIXING SERA FROM PIGEONS IN AVIAN LEUKOSIS. (E.) Watanabe, M. (Natl. Inst. Anim. Hlth., Tokyo, Japan). *Bibl Haemat* 36:183-191, 1970.

Inoculation of pigeons with the Schmidt-Ruppin (S-R) strain of Rous sarcoma virus produced tumors approximately 10 days postinoculation; complement fixing (CF) antibodies to Rous sarcoma virus appeared in pigeon sera by 30 days after inoculation. Tumors regressed by 70 days postinoculation, and the inoculated pigeons were resistant to subsequent injections of S-R virus. While tumor incidence in pigeons inoculated with S-R virus attained 100%, Bryan's standard strain and Bryan's high titer strain of Rous virus produced only a 50% tumor incidence. Birds not developing tumors did not produce detectable CF antibody to Rous sarcoma virus. S-R virus, but not Bryan virus strains, produced foci on pigeon embryo cell monolayers. The presence of CF antigen to Rous sarcoma virus could be used to distinguish chickens with acute lymphomatosis from chickens with Marek's disease.

1967 VIRAL ANTIGENS IN THE BAI STRAIN A (AVIAN MYELOBLASTOSIS) VIRUS ASSOCIATED MYELOBLASTS AND CHICK EMBRYO FIBROBLASTS. (E.) Rao, P. R. (Postgrad. Ctr., Marangal, India). *Curr Sci* 40(4):81-83, 1971.

Chick embryo fibroblast cultures were infected with a multiplicity of 100 avian myeloblastosis virus particles/cell; myeloblast cells of leukemic chickens were used to prepare soluble fractions which were reacted with antisera against avian myeloblastosis virus and group specific hamster antiserum for 48-72 hr. The myeloblast soluble fraction revealed 2 precipitin lines with the hamster serum, one of which showed identity with the respective single lines observed with chick tissue-absorbed sodium deoxycholate and sodium dodecyl sulfate rabbit sera. Unabsorbed sodium deoxycholate chick tissue showed 2 distinct and 1 very faint line formed against the unabsorbed sodium dodecyl sulfate rabbit serum; only 1 of the lines formed against both unabsorbed sera was continuous with the single line produced against the absorbed sera. In comparison, only 1 precipitin line formed against all sera and each line showed identity with the next one in the case of fibroblast soluble fraction. These results indicated a difference between the viral antigens present in the myeloblast and fibroblast cells despite infection with the same virus.

1968 IMMUNIZATION BY THE RADIATION LEUKEMIA VIRUS. (E.) Harari-Ghera, N. (Weizmann Inst. Sci., Rehovoth, Israel). *Bibl Haemat* 36:261-266, 1970.

Mice were immunized by inoculation with 10⁻²-10⁻⁵ dilutions of radiation leukemia virus (virus obtained from non-leukemic tissues of irradiated mice) and subsequently challenged with leukemic cell isotransplants. One million leukemic cells injected 30 days

after inoculation with radiation virus failed to grow in mice immunized by radiation virus dilutions of 10^{-2} and 10^{-3} injected directly into the thymus, while a 95% tumor cell take was seen in the control group of non-immunized mice. Non-immunized mice given leukemic cell isografts and 400 r whole body irradiation 2 days later showed 100% tumor cell takes. Mice immunized with radiation virus were rendered resistant to leukemic cell challenge at about 2 wk after radiation virus inoculation into the thymus, and this immunity was maintained for as long as 12 wk. Removal of the thymus after immunization with radiation virus did not impair the immunity of immunized mice. Immunization with radiation virus also protected mice against development of lymphoma; an 18% lymphoma incidence was observed following immunization with radiation virus, while nonimmunized mice given whole body irradiation developed lymphoma in 85% of cases.

- 1969 ACTIVITIES OF IMMUNE LYMPHOID CELLS AGAINST LEUKEMIA VIRUS-CARRIER MURINE NEOPLASTIC CELLS. (E.) Sinkovics, J. G. (U. Texas M. D. Anderson Hosp. Tumor Inst. Houston), R. J. Pienta, M. J. Ahearn, J. M. Trujillo and F. M. Mikulik. *Bibl Haemat* 36:618-623, 1970.

Immune lymphocytes were drawn from Swiss mice which rejected implants of lymphoma or sarcoma cells carrying Rauscher leukemia virus antigens. These lymphocytes could not suppress the growth of lymphoma or sarcoma cells *in vitro*. In contrast, delayed growth of tumors and in some cases complete rejections of tumors were observed in mice inoculated with immune lymphocytes mixed with sarcoma or lymphoma cells in proportions of 200 immune lymphocytes to 1 neoplastic cell. Normal lymphocytes failed to impair tumor growth *in vivo*.

- 1970 IMMUNOLOGICAL AND GENETIC FACTORS IN MURINE VIRUS-INDUCED LEUKEMIA. (E.) Chieco-Bianchi, L. (Div. Cancer Res., U. Padua, Italy), D. Collavo, N. Pennelli and G. Tridente. *Bibl Haemat* 36:234-239, 1970.

One group of 1- to 3-day-old mice of C3Hf/Gs (H-2^k), C57BL(H-2^b) and (C3Hf/Gs x C57BL)F1 strains were injected s.c. with 0.05 ml of 20% cell-free extract from C3Hf/Gs mice with passage A Gross virus-induced primary leukemia; a second group of adult C3Hf/Gs and F1 hybrids, both neonatally virus-injected and normal, were given i.p. repeated injections of dilute cell-free leukemic extract containing passage A Gross virus for the preparation of sera against target C3Hf/Gs passage A leukemic cells. Results showed that while serum from C3Hf/Gs mice that were neonatally virus-injected and immunized when adults contained practically no antibodies, the serum from C3Hf/Gs mice receiving no virus neonatally but immunized when adults showed significant antibody titers. Sera taken from 2 F1 hybrid groups exhibited a remarkably similar cytotoxic activity regardless of the fact that one group had been treated with virus neonatally and the other group remained untreated.

All these sera were devoid of detectable cytotoxicity when tested on normal C3Hf/Gs cells as were sera from normal C3Hf/Gs and F1 hybrid donors when tested on leukemic C3Hf/Gs cells. The oncogenic effect of passage A group virus was neutralized by sera from both C3Hf/Gs and F1 hybrid mice which had received virus when adults; serum from F1 hybrids neonatally virus-injected and immunized when adults was equally effective and showed a remarkable decrease in leukemia incidence in the test animals; serum from C3Hf/Gs mice, neonatally injected with virus and subsequently immunized did not neutralize the oncogenicity of the virus.

- 1971 THE ACTION OF DNA ANTAGONISTS ON EPSTEIN-BARR VIRUS (EBV)-ASSOCIATED EARLY ANTIGEN (EA) IN BURKITT LYMPHOMA LINES. (E.) Gergely, L. (Karolinska Inst., Stockholm, Sweden), G. Klein and I. Ernberg. *Int J Cancer* 7(2):293-302, 1971.

The effect of cytosine arabinoside (200 μ g/ml and iododeoxyuridine (1-100 μ g/ml) on Epstein-Barr virus-associated antigens was studied in two Burkitt lymphoma-derived carrier culture lines by combined immunofluorescence and autoradiography (³H-thymidine). Early antigen (EA)-positive cells accumulated in treated cultures at a concentration 5-40% in response to both drugs compared to 2% in untreated cultures; cytosine arabinoside blocked production of viral capsid antigen more effectively than iododeoxyuridine, and in both lines virtually all viral capsid antigen positive cells were EA-antigen positive also. It has been suggested that EA is a prerequisite for viral capsid antigen.

- 1972 ANTIBODIES TO EPSTEIN-BARR VIRUS IN A BURKITT'S LYMPHOMA CELL LINE IN TAIWAN MONKEYS (*MACACA CYCLOPIS*). (E.) Chu, C. T., (Coll. Med., Natl. Taiwan U., Formosa), C. S. Yang and A. Kawamura, Jr. *Appl Microbiol* 21(3):539-540, 1971.

Indirect immunofluorescence tests indicated that of 273 adult Taiwan monkeys (*Macaca cyclopis*) 193 or 70.7% harbored anti-Epstein-Barr virus antibody at titers of 1:10 or less, while 1 had a titer of 1:640. Healthy persons in Taiwan had a peak anti-Epstein-Barr virus antibody titer of 1:160. To determine the persistence of maternal anti-Epstein-Barr virus antibody in baby Taiwan monkeys, blood specimens were collected at 5 wk intervals from 6 monkeys which had been separated from their mothers at birth and fed artificially. Two baby monkeys had low antibody titers for 50 wk, indicating a long persistence of the maternal antibody in some cases.

- 1973 ANTIBODIES TO EARLY EPSTEIN-BARR VIRUS-INDUCED ANTIGENS IN BURKITT'S LYMPHOMA. (E.) Henle, G. (Child. Hosp. Philadelphia, Pa.), W. Henle, G. Klein, P. Gunven, P. Clifford, R. H. Morrow and J. L. Ziegler. *J Nat Cancer Inst* 46(4):861-871, 1971.

Antibodies to early Epstein-Barr virus-induced antigens (EA) and other Epstein-Barr virus-related antigens were compared, and the significance of anti-Epstein-Barr antigens in Burkitt's lymphoma was investigated in sera from African patients with clinically and histologically confirmed Burkitt's lymphoma. The results of EA tests showed positive reactions in sera which had anti-Epstein-Barr virus-related antigen titers of at least 1:40; however, sera with titers of this magnitude of anti-Epstein-Barr virus-related antigen did not always contain the EA antigen. Not every patient with Burkitt's lymphoma had antibodies to EA antigen and of 17 patients admitted without detectable antibodies, 59% survived for one year; of those who had titers greater than 1:40 at admission, only 28% survived a year. Most sera obtained shortly before death had high titers in contrast to those who had survived for 2 yr or longer in which the antibody was lacking or the titer was low. The differential responses of Burkitt's lymphoma patients remains unexplained.

974

SEROEPIDEMIOLOGIC STUDIES OF EPSTEIN-BARR VIRUS ANTIBODY IN MONKEYS. (E.)

Anderson, J. C. (Bionetics Res. Lab., Inc., Kensington, Md.) and L. B. Malan. *J Nat Cancer Inst* 46(4): 881-884, 1971.

Indirect immunofluorescence tests were performed on sera from a colony of Macaque monkeys (*Macaca mulatta* and *M. fascicularis*) to detect the presence of antibodies to the Epstein-Barr virus in these animals. All adult breeder monkeys had positive antibody titers; all of 30 newborn monkeys had positive antibody titers. However, the number of animals having positive titers dropped as the age of the monkeys tested increased; 3% of 3-month-old animals and less than 5% of 8-10-month-old animals had positive antibody titers. No antibody was found in macaques 18-20-month old. Of 10 4-yr-old macaques tested, 3 had positive antibody titers. Seronegative monkeys exposed to the breeding colony of monkeys showed positive virus antibody titers in 3 of 20 cases within 6 months of exposure.

975

SEROLOGICAL STUDIES OF THE FELINE LEUKEMIA VIRUS. (E.)

Hardy, W. D., Jr. (Sloan-Kettering Inst. Cancer Res., New York, N.Y.), G. Geering, J. J. Old, E. De Harven, R. S. Brodey and S. K. McDonough. *Bibl Haemat* 36:343-354, 1970.

Antiserum to group-specific antigen of feline leukemia virus was prepared in a female New Zealand white rabbit from tissue washings and pleural fluid of a male domestic cat with lymphosarcoma; antisera to murine leukemia virus group-specific antigens were prepared in rats with Gross virus-induced leukemia transplants of an inbred rat. After suitable absorption, the rabbit anti-feline leukemia virus serum reacted with antigen present in tissue extracts from 75% of lymphomatous cats and in the salivary glands of 4 of the 33 lymphomatous cats tested. In control tissue extracts from 46 normal cats and cats with diseases

other than lymphosarcoma, feline leukemia virus antigen was detected in the tissue extracts of one ostensibly healthy cat; 5 of 13 cases of infectious peritonitis possessed the antigen, and 2 cats with spontaneous fibrosarcoma contained the antigen and C-type virus particles. Neoplastic tissues from 2 dogs with lymphosarcoma after receiving feline leukemia virus at birth demonstrated the antigen and budding leukemia virus. Other species examined including dog, cow, pig, goat and man were negative for the presence of the antigen. The milk of 27 normal lactating cats was also negative for feline leukemia virus antigen.

1976

COMPARATIVE STUDIES OF FELINE AND HUMAN LEUKEMIA BY MIXED HEMADSORPTION REACTION.

(E.) Maruyama, K. (U. Texas M. D. Anderson Hosp. Tumor Inst., Houston), L. Dmochowski and C. G. Rickard. *Bibl Haemat* 36:355-367, 1970.

Two tissue culture cell lines (F-491 and F-503) derived from bone marrow specimens of cats with virus-induced lymphoma and a culture cell line (FE-4) derived from a normal cat embryo and treated with a cell-free filtrate of homogenate of tumor tissue from a Siamese cat with spontaneous lymphoma, as well as cell lines derived from human embryonic kidney and infected *in vitro* with Rauscher leukemia virus, human embryonic skin and whole human embryo, were used to study the hemadsorption reaction with anti-murine leukemia virus immune sera and with human sera. Results of mixed hemadsorption tests and electron microscopy of feline cell cultures from virus-induced lymphomas were positive with anti-murine leukemia virus, anti-Rauscher leukemia virus (monkey), and anti-rat-adapted Friend leukemia virus; numerous type C particles and budding appeared in the cultures. Controls were negative when tested with anti-murine leukemia virus serum and one culture gave positive results with anti-Rauscher leukemia virus monkey serum and anti-rat-adapted Friend leukemia virus rabbit serum; a small number of type C particles were found in this last culture by electron microscopy. The results of tests of feline cell cultures with human sera showed the incidence of positive tests to be higher with sera from normal individuals than with sera from patients with leukemia, lymphoma or other neoplastic diseases, with no significant difference between virus-infected cultures and a control non-infected culture. Both monkey and mouse immune sera against mouse Rauscher leukemia virus gave positive reactions at titers of 1:1024 and 1:256, resp., when tested with virus-infected human embryo kidney cells; control tissue gave negative reactions. Rabbit immune serum against rat-adapted Friend leukemia virus was also positive at a titer of 1:256 with the infected cell line, but negative with the non-infected cell line. Monkey immune serum against HeLa cells gave a titer of 1:2048 with both culture lines, while mice immune sera against feline embryo cultures infected with feline lymphoma virus were positive with both infected and uninfected human cultures; numerous type C particles and budding were found in the infected culture. Three of 20 sera of leukemia patients of various types gave positive reactions when tested against Rauscher leukemia virus-infected human embryo kidney cells at a titer varying from 1:8 to 1:32, whereas none of the 20 normal donor sera gave positive reactions.

IMMUNOLOGY

- 1977 FELINE LEUKEMIA VIRUS: DETECTION OF GROUP-SPECIFIC VIRAL ANTIGEN AND INFECTIOUS VIRUS BY A COMPLEMENT FIXATION TEST. (E.) Sarma, P. S. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), J. F. Baskar, R. J. Huebner, L. J. Old and W. D. Hardy, Jr. *Bibl Haemat* 36:368-378, 1970.

Hyperimmune antiserum prepared in rabbits with ether-disrupted feline leukemia virus was used to detect complement fixation antigens in feline lymphosarcoma, osteosarcoma and fibrosarcoma tissues; this test was utilized for detection of the replication of feline leukemia and sarcoma viruses in susceptible feline embryo fibroblast cultures. Feline embryo fibroblast cultures inoculated with field specimens of feline lymphosarcoma such as clarified tissue extracts, clarified body fluids, and partially purified tumor concentrates developed antigen titers of 1:4 to >1:32 within 10-12 days after viral inoculation, whereas parallel uninoculated control cultures failed to react with rabbit antiserum (titer 1:4). Electron microscopy and radioisotope labeling techniques gave parallel results.

- 1978 INACTIVATION OF T ANTIGEN-FORMING CAPACITIES OF SIMIAN VIRUS 40 AND ADENOVIRUS 12 BY ULTRAVIOLET IRRADIATION. (E.) Yamamoto, H. (Natl. Inst. Hlth., Tokyo, Japan), and H. Shimojo. *J Virol* 7(4):419-425, 1971.

Monolayers of primary or secondary cultures of green monkey kidney cells and human embryonic kidney cells were inoculated with 0.2 ml of UV-irradiated or non-irradiated simian virus 40 and adenovirus 12, resp. After adsorption at 36°C for 2 hr, the cell cultures were incubated at 36°C for 72 hr (simian virus 40) or 48 hr (adenovirus 12) in medium containing cytosine arabinoside, the number of cells were counted under a fluorescence microscope and later examined again following incubation with anti-simian virus 40 serum. The appearance of T antigen-positive cells was slower in cultures infected with UV-irradiated viruses than with unirradiated viruses. The percentage of T antigen-positive cells in green monkey kidney cells for all cells increased up to 72 hr postinfection and then remained unchanged whereas in human embryonic kidney cells, T antigen-positive cells increased up to 48 hr and then decreased. A linear relationship was always observed in repeated experiments when the percentage of T antigen-positive cells was less than 10% in the dose-response curve. In contrast to the unirradiated virus, irradiated virus of both groups induced T antigen in more cells than expected when cells were infected with lower dilutions of virus suggesting that multiplicity reactivation may have occurred in cells infected with UV-irradiated virus at a higher multiplicity. Irradiation of the viruses resulted in inactivation of T antigen-forming capacities of both viruses at the same rate as their infectivities.

- 1979 ATTEMPTS OF IMMUNIZATION AGAINST TUMORS INDUCED BY SV40 VIRUS IN HAMSTERS. (Fr.) Ciobanu, Z. (Dr. I. Cantacuzino Inst., Bucharest, Rumania) and A. Fenyves. *Arch Roum Path Exp Microbiol* 29(1-2):109-116, 1970.

Hamsters immunized by SV40-transformed and irradiated hamster cells developed tumors in 87.5% of cases following challenge with cells from tumors induced in hamsters by inoculation of transformed cells or of SV40. Hamsters immunized with a high-titer strain of SV40, by contrast, developed tumors in only 30% of cases following tumor cell challenge. Thirty to ninety day-old hamsters given a highly tumorigenic dose of SV40 at birth were rendered almost completely immune to tumor development by 1 or 2 doses of the high-titer virus. Immunization of female hamsters 1-3 months before parturition with the high titer SV40 protected their offspring from tumor induction by SV40 injection.

- 1980 STUDIES ON NONDEFECTIVE ADENOVIRUS-SIMIAN VIRUS 40 HYBRID VIRUSES: I. A NEWLY CHARACTERIZED SIMIAN VIRUS 40 ANTIGEN INDUCED BY THE Ad2⁺ND₁ VIRUS. (E.) Lewis, A. M., Jr. (Natl. Inst. Allerg. Infect. Dis., Natl. Inst. Hlth Bethesda, Md.) and W. P. Rowe. *J Virol* 7(2):189-197, 1971.

The distribution of simian virus 40 (SV40) "U" antibody (heat-stable) in hamsters bearing SV40 induced tumors and the induction of the U antigen by the nondefective adenovirus 2-SV40 hybrid virus (Ad2⁺ND₁) and SV40 viruses was studied in weanling hamster kidney cell cultures and SV40-transformed human fibroblasts by complement fixation. In tumor-bearing animals, antibodies to SV40 T antigen first appeared when tumors were 10-25 mm in diameter and antibody to SV40 U antigen developed 1-3 wk later. At 100 days after injection when the tumors were 40-50 mm in diameter, T antibody titers were between 1:40 and 1:320, whereas U antibody titers ranged from less than 1:10 to 1:160. Cells infected with or transformed with SV40 contained 4-64 units of heat-stable SV40 antigen which reacted only with the T⁺ U⁺ hamster pool and 16-128 units of heat-labile SV40 T antigen which reacted with both T⁺ U⁺ and T⁺ U⁻ serum pools. In response to treatment with cytosine arabinoside and heat adenovirus 2 V antigen was completely inhibited, and the appearance of SV40 U antigen in hybrid cells was delayed for approximately 4 hrs; the number of cells containing the antigen was reduced 20-fold. Since SV40 U antigen is present in both tumors and transformed cells, it could be involved in SV40-mediated transformations.

- 1981 IMMUNOFLUORESCENT STUDIES OF ANTIGENS INDUCED BY ADENOVIRUS TYPE 12. (E.) Srivastava, P. (Med. Coll. Georgia, Augusta) and S. S. Lefkowitz. *Proc Soc Exp Biol Med* 136(4):1133-1140, 1971.

Guinea pigs were immunized sequentially with purified adenovirus type 12 and equal amounts of complete Freund's adjuvant as a first injection and incomplete Freund's adjuvant as a second injection 1 wk later. They were bled 2 wk following the final injection as a source of antibody to viral antigens while antisera to T antigens were obtained from hamsters bearing either transplanted or virus-induced tumors.

La cells infected with adenovirus type 12 were sensitive for T antigens as determined by immunofluorescent techniques 6 hr after viral adsorption primarily within the nuclei of infected cells, with smaller amounts appearing within the cytoplasm. The number of cells and the intensity of fluorescence increased until 24 hr postinfection followed by a decrease by 72 hr. A second type of fluorescence, termed fluorescent dots, was first noted 16-18 hr after viral infection only in the nuclei of infected cells and were morphologically distinct from the dots previously reported. Fluorescence intensity and the number of cells affected became maximal by 48 hr, followed by a decrease again at 72 hr. Viral antigens were first noted within the nuclei of infected cells at 18-20 hr and gradually increased in size until the nuclei became filled with large amounts of the brilliantly stained antigens. A fourth antigen, the fluorescent membranes, was not found at 48 hr after viral infection but could be detected at 72 hr; the number of cells demonstrating this antigen increased up to 72 hr. No specific fluorescence was seen in control preparations, although some faint autofluorescence was noted. Most of the hamster sera reacted with antigens; however, less than 50% of these sera reacted with the exclusively intranuclear antigen and the antigen found at the cell membrane.

2 CONCOMITANT IMMUNITY IN HAMSTERS BEARING SYNGENEIC TRANSPLANTS OF TUMORS INDUCED BY PARA-ADENOVIRUS 7, SIMIAN ADENOVIRUS 7, 9,10-DIMETHYLBENZANTHRACENE. (E.) Lausch, R. N., Milton S. Hershey Med. Ctr. Pennsylvania St. U., Hershey) and F. Rapp. *Int J Cancer* 7(2):322-330, 1971.

Animals were induced in mice by s.c. injection of 2-dimethylbenz(a)anthracene (DMBA) or simian adenovirus 7 (SA7) and transplanted into other mice; 1 wk thereafter, transplant-bearing mice were given a second transplant of DMBA- or virus-induced tumor cells to test the resistance to the second transplant conferred on the mice by the first transplant. In mice bearing palpable DMBA-induced tumor transplants which were challenged 1 wk later by DMBA-induced tumor cells, the growth of the second transplant was delayed and the number of cells required to produce tumors in 50% of mice was 10 times greater than in tumor-free controls. Although the initial tumor transplant apparently rendered mice immune to subsequent transplants, the primary tumor transplant grew progressively in these mice. In a related experiment, a less transplantable DMBA-induced tumor line was inoculated into mice prior to challenge with cells of the same tumor; the total tumor incidence produced by s.c. injection with tumor cells in tumor-free mice was 58%, while that in mice already inoculated with tumor cells was 13%. Resistance to a second tumor transplant was found to be specific with tumor cells induced by SA7 virus and A-adenovirus 7 and DMBA-induced tumor cells.

3 PASSIVE TRANSFER OF TUMOR-SPECIFIC RESISTANCE TO METHYLCHOLANTHRENE-INDUCED SARCOMAS IN RATS. (E.) Ishikawa, Y. (Hiroshima U. Sch.

Med., Japan), M. Fukushima, T. Sato, M. Komaba, H. Yagihashi, A. Hokama and M. Kojika. *Tohoku J Exp Med* 103(2):195-201, 1971.

Sarcomas were induced in rats by s.c. injections of methylcholanthrene (10 mg); tumors were excised, and the tumor cells were injected into the same rats from which they had been taken, as well as into another group of rats (the donors). Sensitized spleen cells were prepared from these donor rats, and spleen cell supernates were injected i.p. into the rats whose tumor cells had originally been used to sensitize the donors. The antitumor activity of the splenic supernate was judged by the number of days from the time of excision of the original tumor to the death of the rat. Control rats (those given injections of tumor cells immediately after excision of the original methylcholanthrene-induced tumor, but not given spleen cells from sensitized donors) showed survival times of 27-47 days; the average weight of excised tumors at the death of these rats was about 3 g. Rats given sensitized spleen cells had survival times of 22-101 days, and final tumor weights of about 3 g. The survival of sensitized spleen cell-recipient rats was significantly prolonged relative to the survival of controls.

1984 IMMUNOTHERAPY EXPERIMENTS WITH A METHYLCHOLANTHRENE-INDUCED GUINEA PIG LIPOSARCOMA. (E.) Eilber, F. R. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), E. C. Holmes and D. L. Morton. *J Nat Cancer Inst* 46(4):803-808, 1971.

The effect of intradermal immunization with syngeneic tumor cells on the growth of methylcholanthrene-induced liposarcoma was studied in strain-2 guinea pigs. Immunization with viable tumor cells inadequate to produce progressively growing tumors with or without Bacillus Calmette-Guerin (BCG) as an adjuvant completely prevented the subsequent growth of the i.m. challenge tumor. In contrast, 88% of the nonimmunized controls developed progressively growing tumors. Prior sensitivity to BCG did not affect the subsequent growth of intramuscular tumor cells. Viable cells from grafts of the transplanted tumor, irradiated tumor cells and tumor cells grown in tissue culture were effective as immunogens. These studies indicated that tumor-specific transplantation antigens can be used for immunotherapy of a chemically induced sarcoma in syngeneic guinea pigs. Use of these antigens for clinical immunotherapy of patients with a limited number of residual tumor cells is at least theoretically possible.

1985 CROSS-REACTING TUMOR-SPECIFIC TRANSPLANTATION ANTIGENS IN METHYLCHOLANTHRENE-INDUCED GUINEA PIG SARCOMAS. (E.) Holmes, E. C. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), D. L. Morton, G. Schidlovsky and E. Trahan. *J Nat Cancer Inst* 46(4):693-700, 1971.

The characteristics of tumor-specific transplantation antigens in methylcholanthrene (MCA)-induced guinea pig sarcomas were studied utilizing electron microscopy. Animals immunized by temporary growth with either

IMMUNOLOGY

MCA-A or MCA-C liposarcomas resisted both MCA-A or MCA-C liposarcomas when simultaneously challenged with these tumors with no MCA-A tumor takes and only 1 MCA-C tumor take occurring in 6 immunized guinea pigs, compared to 100% incidence growth in untreated control animals. However, in all MCA-A and MCA-C resistant guinea pigs tumor MCA-25 grew progressively, indicating that MCA-25 contained an individually distinct tumor-specific transplantation antigen, whereas MCA-A and MCA-C contained similar tumor-specific transplantation antigens. Electron microscopic examination revealed virus-like particles in the tumor cells of MCA-A and MCA-25 but failed to reveal any in MCA-C cells.

- 1986 TUMOR-SPECIFIC ACTIVE ENHANCEMENT OF A MURINE SARCOMA. (E.) Bloom, E. T. (Dept. Med. Microbiol. Immunol., U. California, Davis) and W. H. Hildemann. *Tissue Antigens* 1(1):5-13, 1971.

Mice of the C57Bl/10 strain were immunized with 10^6 viable sarcoma cells from a mouse sarcoma induced by 3-methylcholanthrene and subsequently challenged with inocula of sarcoma cells of the same type. Growth of transplanted sarcoma cells in preimmunized animals was much accelerated compared to the growth of sarcomas in unsensitized mice; by day 15 after challenge with sarcoma cells, mean tumor volumes in unsensitized mice were 0.42 cc and in preimmunized mice were 0.98 cc; the relative figures for tumor volume in sensitized and control mice on day 27 were 5.0 and 2.5 cc, resp. It was shown that the accelerated tumor growth following pre-immunization was tumor-specific and not a result of non-specific weakening of the host defenses. The growth of sarcomas could also be enhanced by pretreating mice with anti-sarcoma antiserum. Enhancement of tumor growth was more consistently induced in male than in female mice.

- 1987 INFLUENCE OF AMOUNT OF ANTIGEN ON IMMUNITY INDUCED BY SPECIFIC ANTIGENS OF SOLID SYNGENIC MOUSE TUMORS. (Fr.) Donner, M. (Res. Unit Exp. Cancerology, Tumoral Radiobiol., Vandoeuvreles-Nancy, France) and C. Burg. *C R Soc Biol* 164(8-9): 1832-1836, 1970.

Rhabdomyosarcomas RV₂ and CB 1 were induced by methylcholanthrene, resp., in male and female C₃H/He mice which were then immunized by s.c. inoculation of 2×10^{-3} mg to 500 mg tumor fragments sterilized by X-irradiation. RV₂ tumors occurred in about 80% of the animals. There was a perceptible diminution in rate of tumor formation after immunization with 500 mg of irradiated tumor cells. Mean survival and mean tumor diameter showed no significant differences in the various animal groups. In animals with CB 1 tumors, the degree of immunization varied with the dose of irradiated tumor tissue. Optimal resistance occurred at doses in the neighborhood of 1 mg. When the dosage was greater than 1 mg, tumor growth increased significantly compared to untreated animals. Survival of the immunized animals was not significantly different from untreated animals.

- 1988 TRANSFER OF TUMOR-SPECIFIC IMMUNITY WITH RNA: INHIBITION OF GROWTH OF MURINE TUMOR ISOGRAFTS. (E.) Ramming, K. P. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and Y. H. Pilch. *J Nat Cancer Inst* 46(4):735-750 1971.

C3Hf/HeN mice were injected in the right hind limb with 0.1 ml of tumor cell suspensions from BP-1 or BP-4 benzopyrene-induced sarcomas, and the limb was amputated after tumor formation. Ten days post-amputation, the mice were given s.c. injection of 10^4 viable cells of the same tumor used for immunization, while normal mice received 10^4 BP-1 or BP-4 sarcoma cells as controls. Extracts rich in RNA were prepared from spleens and lymph nodes of Hartley guinea pigs 10-14 days after immunization with C3H BP-4 sarcoma and labeled; groups of 20-30 normal C3H/HeN mice were challenged with i.p. injections of 0.5 ml spleen cells incubated with a) RNA from lymphoid tissues of guinea pigs immunized with BP-4 mouse sarcoma (BP-4 RNA); b) RNA from guinea pigs immunized with BP-1 sarcoma (BP-1 RNA); c) RNA from pigs immunized with normal C3H tissues (normal tissue RNA); d) RNA from pigs given Freund's adjuvant only (Freund's adjuvant RNA); e) BP-4 RNA treated with ribonuclease; f) BP-4 RNA treated with deoxyribonuclease; or g) BP-4 RNA treated with pronase. Tumor incidence in mice challenged with tumor cells similar to immunization amounted to 0% and 9% for BP-4 and BP-1 sarcoma cells, resp., compared to controls of 78% and 97% tumor incidence, resp., whereas those challenged with tumor cells BP-1 and immunized against BP-4 and vice versa showed a tumor incidence of 79% and 77% and in controls, 87% and 75% resp. Recipients of spleen cells incubated with BP-4 RNA had a significantly lower incidence of tumor development than did mice in any other group; spleen cells incubated with RNA from guinea pigs immunized with normal C3H mouse tissues did not inhibit tumor development; those receiving spleen cells incubated with RNA from pigs immunized with Freund's adjuvant alone did not evidence decreased tumor incidence. Similar results occurred with injection of syngeneic spleen cells alone, whereas those receiving cells incubated with BP-4 RNA ribonuclease-treated preparation had a tumor incidence similar to that of the challenge controls. Inactivation did not occur in response to treatment with deoxyribonuclease or pronase.

- 1989 SYNERGISTIC IMMUNODEPRESSIVE EFFECT OF 7,12-DIMETHYLBENZ[a]ANTHRACENE AND URETHAN IN THE RAT. (E.) Perocco, P. (Inst. Gen. Path., Bologna, Italy), C. Franceschi, A. T. Di Marco and G. Prodi. *Proc Soc Exp Biol Med* 136(4):1024-1026 1971.

The effects of combined doses of 7,12-dimethylbenz[a]anthracene (DMBA) and urethan on the hemagglutination titers achieved by the rat immune system in response to human red blood cell antigen were investigated. Male rats were given i.p. doses of DMBA (5-50 µg, body wt) followed by 6 successive i.m. doses of urethan (0.1-1.0 mg/g body wt); 8 days after the beginning of treatment, rats were given 1 ml/100

dy wt of human RBC. Neither DMBA nor urethan affected the hemagglutinin response of the rats to the antigen; control rats not given carcinogen showed hemagglutinin titers of 7.70 (\log_2 of the inverse of the maximum dilution showing an appreciable hemagglutination), and rats given either carcinogen alone showed titers of 7.40-7.55. DMBA and urethan administered concurrently, however, depressed the hemagglutination titers; larger doses of carcinogens produced more marked depression of the response. Rats given 25 $\mu\text{g/g}$ DMBA and 0.5 mg/g urethan showed hemagglutinin titers of 3.80. Double treatment with carcinogens failed to prolong the survival of skin grafts against a weak histocompatibility barrier.

1990 THE ANTIGENICITY OF RAT MAMMARY TUMOURS INDUCED BY 7,12-DIMETHYLBENZ(a)ANTHRACENE.

(E.) Kellen, J. A. (Banting Inst., U. Toronto, Ontario, Canada) and K. M. Anderson. *Oncology* 18(1):49-54, 1971.

The antigenic properties of a histologically diverse group of 7,12-dimethylbenz(a)anthracene-induced rat mammary gland tumors were studied by means of double-diffusion agar techniques. Antisera harvested from immunized rabbits showed effective titers persisting for a period not exceeding 3 wk; the unabsorbed sera reacted with all 17 tumor extracts, usually within 24 hr in sharp precipitation bands with a single line appearing followed by a second, and sometimes a third. The reactivity of the antisera had no relation to the tumor size, rate of growth and histopathology. No cross-reaction with normal rat organs or serum occurred.

1991 MORPHOLOGICAL AND IMMUNOCHEMICAL STUDIES OF RAT GLIAL TUMORS AND CLONAL STRAINS PROPAGATED IN CULTURE. (E.) Benda, P. (Massachusetts Gen. Hosp., Boston), K. Someda, J. Messer and W.H. Sweet. *J Neurosurg* 34(3):310-323, 1971.

The establishment of stable permanent lines of transplantable glial tumors induced in Wistar strain and C.D. Fisher rats by injections of N-nitrosomethylurea were studied by means of culture propagation and light, phase and electron microscopic techniques. Within a few days after the start of N-nitrosomethylurea injections, between 17-43 wk after termination of injections, primary brain tumors and 3 schwannomas were found among 60 Wistar rats and 3 primary and 1 s.c. type have been successfully maintained in culture for 3 yr. Among 48 C.D. Fisher rats, 10 primary brain and 1 primary cord tumor were found; 7 of these were successfully subcultured over a period of a yr. Inoculation of dispersed cell aliquots (106 cells) from each of the 11 lines into newborn rats resulted in visible localized tumor within 2-3 wk under the skin, muscle, or in the peritoneal cavity according to the site of injection with no evidence of metastases. In C.D. Fisher rats, neoplasms rapidly increased in size, were firm and had a homogeneous texture under a scalpel capsule; in Wistar rats necrosis occurred centrally with or without fluid formation as the necrosis extended, and after intracranial injection

the brain section surface was covered by an extensive tumor mantle. Primary tumors were generally composed of undifferentiated cells with tumor satellitosis, while secondary tumors varied according to the site of inoculation. The distinctive neural protein called "S-100" was detected in soluble extracts of cultured cells from both primary and secondary tumors. If the cloned cultures maintain relative invariability of growth rate and degree of differentiation the value of this rat model in the study of the metabolism, radio-sensitivity, and chemotherapy of gliomas will exceed that of any others currently known.

1992 TUMOR IMMUNITY: IMPAIRMENT IN TUMOR-BEARING HOSTS. (E.) Bernstein, I. D. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), H. T. Wepsic, B. Zbar and H. J. Rapp. *J Nat Cancer Inst* 46(4):873-880, 1971.

Strain-2 guinea pigs were initially immunized against a diethylnitrosamine-induced hepatoma by inoculation with living hepatoma cells; ascites and solid tumors of 3 different lines were used. Cell-mediated systemic tumor immunity was transferred passively from immunized donors to unimmunized syngeneic recipients by inoculating guinea pigs with peritoneal exudate from immunized animals following an initial tumor-inducing dose of tumor cells prior to tumor cell challenge. While tumor-bearing animals showed immunity toward the tumor cell challenge, this immunity, in terms of tumor growth suppression, was significantly less than that of passively immunized tumor-free animals. The impairment of the immune response in tumor-bearing guinea pigs was seen in animals bearing tumors with differing antigenicities. Serum from animals bearing large tumors had no effect on passively transferred tumor immunity. It is believed that successful transfer of systemic tumor immunity depends on factors contributed by the recipient of the tumorigenic transplant.

1993 SURVIVAL OF TUMOURS AFTER IMMUNIZATION AGAINST OESTROGENS (E.) Caldwell, B.

V. (Yale U. Sch. Med., New Haven, Conn.), S. A. Tillson, H. Esber and I. H. Thorneycroft. *Nature* 231(5298):118-119, 1971.

Female rats bearing transplanted estrogen-dependent mammary adenocarcinoma were immunized against estrogens by injection of 1 mg of estradiol-17 β -hemisuccinate; immunizations were performed once a wk for 4 wk with 1 booster injection 4 wk later. The time between implantation of tumor and first signs of tumor growth was 36 days in rats not given active estrogen immunization and 50 days in immunized rats. Immunized rats had a survival time of 100 days compared with a survival time of 60 days for unimmunized rats. Rats showing the highest titers of anti-estrogen antibodies had the longest survival times.

1994 IMMUNOCHEMICAL STUDIES ON ANTI-4-AZOQUINOLINE-1-OXIDE ANTIBODY. (E.) Nakashima, S. (Fac. Pharm. Sci., Toyama U., Gofuku, Japan). *J Biochem* 69(3):605-607, 1971.

Rabbit serum protein was conjugated with diazotized 4-aminoquinoline-1-oxide, and rabbits inoculated with the conjugate yielded antisera containing antibodies to the conjugate. A quantitative precipitation reaction between the rabbit serum protein-4-aminoquinoline-1-oxide conjugate and anti-conjugate antibody was performed. Of the 2 antibody-containing antisera prepared, one precipitated 100 µg of conjugate equal to 14 mg of antibody, and the other precipitated 50 µg of conjugate to equal 10 mg of antibody. 4-Nitroquinoline-1-oxide itself inhibited the precipitation of conjugate by antibody. When 4-nitroquinoline-1-oxide was added to the antibody-conjugate mixture, the amount of precipitate was reduced by 20%. Gel filtration and 2-mercaptoethanol treatment of the antibody revealed that it was of the IgG class.

- 1995 USE OF SARCOMA 180 TO PREPARE HEMAGGLUTININATING AND COMPLEMENT-FIXING ANTIGENS FOR VIRUSES IN ADULT MICE. (E.) Mettler, N. E. (Yale U. Sch. Med., New Haven, Conn.), J. Casals, D. H. Clarke, W. G. Downs and R. E. Shope. *Proc Soc Exp Biol Med* 136(4):1355-1359, 1971.

Mice of both sexes (Charles River CD (R)-1), 4-7 wk old, were inoculated i.p. with 0.2 ml of fresh sarcoma 180 ascitic fluid followed 7-9 days later, after the appearance of abdominal swelling, with i.p. injections of different viruses. Two days after viral inoculation, eastern equine, Mayaro, Sindbis, Una and St. Louis encephalitis viruses produced ascitic fluid hemagglutinins with titers of 1:32 or higher, with highest titers appearing on days 3 or 4, which were shown to be inhibited by the homologous immune fluids. With the remaining 10 viruses tested, ascitic fluids were either negative or, in the case of Hazara, Uukuniemi, and Marituba, gave such low hemagglutinin titers that further characterization was not carried out. Ten of the viruses tested produced satisfactory ascitic fluid complement fixation antigen and comparison of reactivity antigens from mouse brain and liver revealed no marked differences. Regression of the sarcomatous process was observed irregularly in mice inoculated with some of the arboviruses studied. Satisfactory antigens were obtained for arboviruses of groups A, B, C, Phlebotomus fever, Simbu, Uukuniemi, and Congo.

- 1996 STIMULATION OF AUTOCHTHONOUS LYMPHOCYTES BY CELLS FROM NORMAL AND LEUKAEMIC LINES. (E.) Knight, S. C. (New York U. Med. Ctr., New York), G. E. Moore and B. D. Clarkson. *Nature* 229 (6):185-187, 1971.

Lymphoblastoid cell lines derived from 2 leukemic patients were incubated with irradiated autochthonous and allogeneic cells (6000 rads) or with cell lines derived from normal subjects and from a patient with reticulum cell sarcoma. Stimulation of the cells was measured by uptake of tritiated thymidine. Irradiated leukemic cells stimulated both autochthonous cells and normal allogeneic cells to a similar degree. The reticulum cell sarcoma cell line did not stimulate cells from either of the 2 leukemic patients. Both autochthonous and allogeneic irradiated lympho-

blastoid cells stimulated freshly isolated lymphocytes from normal subjects; in 3 of 4 experiments, the stimulation by autochthonous cells was lower than that observed with cells from an allogeneic source. Irradiated autologous lymphoblastoid cells derived from both normal and leukemic individuals stimulated freshly isolated autochthonous cells, suggesting that the factor responsible was not a specific leukemic antigen.

- 1997 INHIBITION BY PHYTOHEMAGGLUTININ OF DNA SYNTHESIS IN CULTURED MOUSE LYMPHOMAS. (E.) Dent, P. B. (Dept. Pediat., McMaster U., Hamilton, Ontario, Canada). *J Nat Cancer Inst* 46(4):763-773, 1971.

When normal mouse spleen cells were exposed to phytohemagglutinin (PHA) in dilutions of from 1:10-1:500, DNA synthesis was stimulated 10- to 100-fold; addition of PHA to cultures of transplantable murine ascites lymphoma induced by Gross virus decreased DNA synthesis. Both stimulation and inhibition of DNA synthesis by PHA were directly correlated with increasing concentrations of the mitogen. Pokeweed mitogen (PWM) rarely inhibited DNA synthesis in the lymphoma cells, and often caused a 2- to 5-fold increase in DNA synthesis in the lymphoma cells. However, PWM did inhibit DNA synthesis in mouse myeloma cells. PHA produced slight increases in RNA synthesis in normal spleen cells, and less pronounced increases in lymphoma cells. It was found that high concentrations of PHA reduced the number of viable cells in both normal and lymphomatous cells, but the lower concentrations had no evident cytotoxicity. PHA-induced inhibition of DNA synthesis in lymphoma cells was reversible; removal of PHA from cultures allowed DNA synthesis in the cells to begin to recover. It was thought that neoplastic cells may have an increased density of mitogen receptor sites on their surfaces.

- 1998 PHYTOHEMAGGLUTININ (PHA)-INDUCED TRANSFORMATION OF LYMPHOCYTES FROM PATIENTS WITH CANCER. (E.) Sutherland, R. M. (London Clinic, Ontario, Canada), W. R. Inch and J. A. McCredie. *Cancer* 27(3):574-578, 1971.

Lymphocytes from 71 patients with cancer, 9 patients hospitalized for surgical procedures but without cancer, and 24 healthy subjects were stimulated with phytohemagglutinin (PHA) in the presence of ³H-thymidine and examined for morphological transformation and rate of nucleic acid synthesis. Cancer patients consisted of patients with lymphoma, leukemia, cancer of the breast and cervix, lung cancer and other cancers. No difference in morphological transformation of lymphocytes stimulated with PHA was noted among patients of different ages. Nucleic acid synthesis in PHA-stimulated cells declined as the age of the patient donating the cells advanced; DNA synthesis in cells from 60-yr-old patients was reduced by more than 50% of the rate of DNA synthesis in cells from 1-yr-old patients, and RNA synthesis was similarly, though not

as markedly, reduced. Morphological transformation of lymphocytes from untreated patients with acute leukemia did not differ significantly from that in the controls. Transformation was significantly reduced in untreated patients with chronic leukemia, and DNA synthesis was slightly reduced in patients with acute leukemia in all stages of the disease. Morphological transformation of lymphocytes from Hodgkin's disease patients in all stages was 75% of control values. Morphological transformation and nucleic acid synthesis were not altered in lymphocytes from untreated patients with carcinoma of the female reproductive system, lung and other cancers.

1999 SUPPRESSION OF CELL-MEDIATED IMMUNITY THROUGH IMMUNE SPLEEN CELLS AGAINST EHR-
LICH ASCITES TUMOR. (E.) Okubo, S. (Nagoya U. Sch. Med., Japan). *Nagoya J Med Sci* 33(4):329-340, 1971.

Twenty test mice and 20 control 60-day-old SMA mice received i.p. injections of 0.2 ml of either immune or nonimmune spleen cell suspension, resp. Seven days later, all animals were challenged s.c. with viable Ehrlich ascites cells. Eleven of 20 mice receiving immune spleen cells 7 days prior to tumor challenge showed progressive growth of the resulting tumor, whereas only 1 of 20 mice receiving nonimmune spleen cells showed progressive growth. Seven of 20 mice in the test group showed tumor growth within a definite period followed by regression, while 19 mice in the control group showed regression after limited growth; regression in the former was slightly retarded in comparison to the latter. Two mice in the test group failed to develop a tumor while none in the control group were without a tumor. In 10 control and 10 test mice, response to tumor formation following injection of viable tumor cells into the foot pads showed that smaller tumors formed in all immunized animals compared to the control group. Mixed tumor and immune or nonimmune spleen cells caused death of all control animals while only 2 of 10 immunized mice succumbed. Serum obtained from mice given immune spleen cells 24 hr previously enhanced the s.c. growth of Ehrlich ascites tumor, whereas serum obtained from mice that had received immune spleen cells 7 days before bleeding did not enhance tumor growth. Tumor enhancement may represent a mechanism by which autochthonous tumors possessing tumor-specific antigens may grow progressively to the death of the hosts.

2000 ANTIGENICITY OF OVARIAN AND CERVICAL MALIGNANCIES WITH A VIEW TOWARD POSSIBLE IMMUNO-
DIAGNOSIS. (E.) Levi, M. M. (Harlem Hosp. Ctr., New York, N.Y.). *Amer J Obstet Gynec* 109(5):689-698, 1971.

Rabbits were injected with tissue culture extracts from ovarian papillary cystadenocarcinoma and cervical squamous cell carcinoma. Ouchterlony double diffusion tests indicated that the antibodies produced were specific and did not cross-react with a variety of other normal and malignant tissues. Iso-

lation of the corresponding antigenic components in tumor tissue was accomplished through Sephadex gel filtration. Tumor tissue was more prevalent than normal tissue in Fraction VI and it is believed that Fraction I contained the antigenic site for the cervical tumor. Further, the antigenic components of the tumors were localized in a high molecular wt fraction. On acrylamide gel electrophoresis, it appeared that the papillary serous cystadenocarcinoma Fractions I and III were low in protein compared to normal human serum. Some evidence exists for believing that the antigens are specific. Immunologic comparison of equivalent fractions eluted from Sephadex gels showed antigenic nonidentity of the fractions derived from normal tissues with those from tumor tissues. Indications are that reproducible and reliable immunotesting procedures can be designed.

2001 DECREASING IMMUNE COMPETENCE AND DEVELOPMENT OF RETICULUM CELL SARCOMAS IN LYMPHATIC TISSUE OF AGED MICE. (E.) Hanna, M. G., Jr. (Oak Ridge Natl. Lab., Tenn.), P. Nettesheim and M. J. Snodgrass. *J Nat Cancer Inst* 46(4):809-824, 1971.

The antigen-trapping capacity of spleen germinal centers in 3 age groups of (C57BL/6 x C3H/An)F₁ (B6C3F₁) mice was studied in relation to the development of reticulum cell sarcoma and the reduction of immunity to test antigen by means of autoradiography. Antigen clearance occurred in the serum of 13-wk-old mice between days 3 and 10 after antigen injection with no comparable clearance occurring in 1.5 and 2.5-yr-old animals. However, clearance was greater in the 1.5-yr-old group than in the 2.5-yr-old animals with a 3-fold decrease in antigen between days 7 and 10 occurring in the first group; in all 3 groups, the relative rates of clearance in the spleen corresponded to those measured in the serum with a marked reduction in the young-adult mice between days 7 and 14. In the young-adult mice at 1 hr after injection with a single dose of ¹²⁵I-human gamma-globulin, label in the spleen was preferentially in the marginal zone of the lymphatic nodules and in active germinal centers or in the cortical lymphoid follicular areas. At 24 hr, the germinal centers were still heavily labeled, and label was concentrated in follicular areas lacking active germinal centers with label decreasing in other areas; in the 18-month-old mice, both the concentration of label per follicle and the total number of labeled follicles were markedly decreased and in the 2.5-yr-old mice, occurrence of germinal centers and/or antigen localization was extremely rare. A 15% increase in non-lymphatic neoplasms in 2.5-yr-old animals with reticulum cell sarcoma was observed in stages 2, 3 or 4 compared to normal, aged animals or to those categorized in stage 1 of the disease. It is not unreasonable to consider that a decrease in immune capacity of the spleen might contribute to the increased frequency of nonlymphatic tissue tumors in these animals.

2002 STUDIES OF CARCINO-FETAL PROTEINS: PHYSICAL AND CHEMICAL PROPERTIES OF HUMAN α -FETOPROTEIN. (E.) Ruoslahti, E. (Dept.

Serol. Bacteriol., U. Helsinki, Finland) and M. Seppälä. *Int J Cancer* 7(2): 218-225, 1971.

The relationship between human α -fetoprotein from serum of human fetuses, fetoproteins from other animals and other human serum proteins was investigated by means of gel electrophoresis and various chemical analyses. The reactive protein in fetal serum to anti- α -fetoprotein was located in the α -fetoprotein band in polyacrylamide gel electrophoresis, which upon purification gave 2 distinct bands with molecular wt of 140,000 and 70,000, resp., and differed from that reported for bovine fetuin at 48,800. Carbohydrate analysis revealed 24.5% contained in fetuin compared to 4.3% in α -fetoprotein. The molecular wt of α -fetoprotein is close to that of albumin and the serum concentrations seem to be inversely related.

2003 IMMUNOFLUORESCENT STUDY OF ALPHA-FOETOPROTEIN (α fp) IN LIVER AND LIVER TUMOURS: I. TECHNIQUE OF α fp LOCALIZATION IN TISSUE SECTIONS. (E.) Engelhardt, N. V. (Gamaleya Inst. Epidem. Microbiol., Moscow, U.S.S.R.), A. I. Goussev, L. Ja. Shipova and G. I. Abelev. *Int J Cancer* 7(2): 198-206, 1971.

Techniques of α -fp detection in normal embryonic liver and human and animal carcinomatous tissue, preparation of purified anti- α -fp antibodies and differentiation of structures containing the protein with those passively incorporating it are described. Paraffin sections of tissues fixed with ethanol and acetic acid revealed a better distribution of the protein than cryostat sections. Dilutions of anti- α -fp h and m antibodies obtained by glutaraldehyde immunosorbent techniques were chosen on the basis of the one giving sufficiently bright reaction with most contrast on sections of human fetal liver. Differentiation of α -fp localization due to uptake rather than production was based on the presence of the protein without the presence of the γ -globulin factor. It is believed that the cellular sites of synthesis of α -fp in embryonal liver are the parenchymal cells and the tumor cells themselves in carcinoma tissue.

2004 IMMUNOFLUORESCENT STUDY OF ALPHA-FOETOPROTEIN (α fp) IN LIVER AND LIVER TUMOURS: II. LOCALIZATION OF α fp IN THE TISSUES OF PATIENTS WITH PRIMARY LIVER CANCER (PLC). (E.) Goussev, A. I. (N. F. Gamaleya Inst. Epidem. Microbiol., Moscow, USSR), N. V. Engelhardt, R. Masseyeff, R. Camain and B. Basteris. *Int J Cancer* 7(2):207-217, 1971.

Sites of specific α fp localization in the tissues of patients with primary liver cancer were studied by immunofluorescent techniques. The concentration of α fp in tumor tissue was considerably less than in blood and comparable to levels found in extracts of tissues from liver, kidney, spleen, lung and pancreas. Two of 7 α fp-positive primary liver cancer cases showed low concentration in blood serum, and antigen was not detected in

tissue specimens by immunofluorescence techniques; in 3 cases the protein was present in liver parenchyma cells simultaneously with γ -globulin antibodies. The antigen was observed in tumor tissue by immunofluorescence in cases of α fp-positive hepatocellular carcinoma. When the concentration in blood serum was 1:64 or more, the tumor sections observed contained both the protein and γ -globulin, supporting the assumption that the site of synthesis was the tumor itself.

2005 SYNTHESIS, ASSEMBLY AND SECRETION OF GAMMA GLOBULIN BY MOUSE MYELOMA CELLS: II. ASSEMBLY OF IgG_{2b} IMMUNOGLOBULIN BY MPC 11 TUMOR AND CULTURE CELLS. (E.) Laskov, R. (Hebrew U. Haddasah Med. Sch., Jerusalem, Israel), R. Lanzerotti and M. D. Scharff. *J Molec Biol* 56(2):327-339, 1971.

Steps in the assembly of IgG_{2b} immunoglobulin after the release of heavy and light chains were studied by pulse-chase experiments with ¹⁴C-labeled valine, threonine and leucine in MPC 11 myeloma cells. The presence of a constant amount of immunologically precipitable material and constant ratio of labeled heavy and light chains between 2-20 min after the chase indicated that no selective degradation occurred. In the first 20 min after the chase, free heavy chains (H), light chains (L), half molecules (HL) and heavy chain dimers (H₂) were the main precursors of the fully assembled IgG (H₂L₂) molecule. A decreased but significant amount (50% of control) of label was incorporated into H₂L₂ in the presence of cycloheximide, indicating that interchain disulfide bond formation occurs after release of the nascent chains from the ribosome. Many half molecules were produced by the tumor cell, but they were not assembled into H₂L₂ and were secreted quantitatively as such or as higher polymers into the medium; the decrease in L, H, H₂ and H₂L accounted for 90% of the increases in fully assembled H₂L₂ and HL. This block in assembly may be due to the presence of a large excess of light chains rather than to a structural defect in the polypeptide chains.

2006 SPECIFICITY AND STRUCTURE OF THE MYELOMA PROTEIN PRODUCED BY MOUSE PLASMACYTOMA MOPC-460. (E.) Jaffe, B. M. (Washington U. Sch. Med., St. Louis, Mo.), E. S. Simms and H. N. Eisen. *Biochemistry* 10(9):1693-1699, 1971.

Balb/c anN mice in which mouse plasmacytomas were induced by serial s.c. transplantation at 3 wk intervals were exsanguinated by cardiac puncture; sera from several transplant generations were pooled and used for isolation and identification of protein MOPC-460. A final yield of purified immunoabsorbed protein 7S amounted to 2.8 mg/ml of serum or 3.95 mg/ml of serum (with an alternate method of determination). The 7S monomer was calculated to have a molecular wt of 150,000 and appeared to consist of 2 light and 2 heavy chains (the light and heavy chains were calculated to be 23,000 and 55,700, resp). In determining ligand binding, MOPC 460 appeared to have a 10-fold greater affinity for dinitronaphthol than for ϵ -DNP-L-lysine.

- 007 ELECTRON MICROSCOPY OF HUMAN AND MOUSE MYELOMA SERUM IgA. (E.) Dourmashkin, R. R. (Natl. Inst. Med. Res., London, England), G. Virella and R. M. E. Parkhouse. *J Molec Biol* 56(1):207-208, 1971.

Immunoglobulin A (IgA) fractionated and purified from the serum of a patient with a secreting myeloma and mouse myeloma IgA, MOPC 315, were examined by electron microscopy. A "double Y" appearance was photographed in most molecules from both specimens; the branching arms appeared more distinct in the mouse fraction compared to the human fraction and was suggestive of a structure consistent with two 7S units, each made up of 2 heavy and 2 light chains, joined together at or near the C-terminal of the heavy chains.

- 008 ELECTRON MICROSCOPY OF COMPLEXES BETWEEN IgA (MOPC 315) AND A BIFUNCTIONAL HAPTEN. (E.) Green, N. M. (Natl. Inst. Med. Res., London, England), R. R. Dourmashkin and R. M. E. Parkhouse. *Molec Biol* 56(1):203-206, 1971.

Mouse myeloma protein, immunoglobulin A (MOPC 315), was isolated as a mixture of unreduced oligomers and was titrated with a bifunctional hapten, bis(DNP-alanyl)-diaminosuccinate, and with a monofunctional hapten, ϵ -DNP-aminocaproate. The bifunctional compound was bound about 10 times as strongly as the monofunctional compound. Electron microscopy revealed the absence of Fab fragments linked to each other. A central, highly contrasted double bar, from the four ends of which extended either a short weakly contrasted projection or a longer arm terminating in a fork, was the most striking feature. Four terminal half molecules, lacking in polymers formed from reduced preparations, appeared to form a tetramer by side-by-side aggregation of two cyclic dimers of the repeating unit or a tetramer in which all four molecules are linked by a hapten to give a cyclic structure. Further experiments should help to clarify the nature of these complexes.

- 009 IMMUNOGLOBULIN SYNTHESIS AND SECRETION: VI. SYNTHESIS AND INTRACELLULAR TRANSPORT OF IMMUNOGLOBULIN IN NONSECRETORY LYMPHOMA CELLS. (E.) Sherr, C. J. (New York U. Sch. Med., New York, N. Y.) and J. W. Uhr. *J Exp Med* 133(4):901-920, 1971.

An established line of Burkitt lymphoma cells (Daudi) synthesizing immunoglobulin M but lacking a well defined endoplasmic reticulum (cultured in fetal calf serum) and an established line of mouse myeloma cells that secrete immunoglobulin G1 (cultured in horse serum) were labeled with ^3H -leucine or ^3H -sugars. The incorporation of labeled-leucine in the mouse myeloma cells was linear throughout the labeling period with a pattern no different from that of other immunoglobulin-secreting cells. However, label incorporation intracellularly was linear for approximately 60 min, followed by a short lag phase when label was secreted into the medium and a "steady state" was reached in 60-120 min. In contrast, Daudi cells incorporated the labeled-leucine into

intracellular immunoglobulin with no evidence of secretion into the medium even after a 6 hr period. The percentage of newly synthesized protein was 1-2% as compared to 20% in the mouse myeloma cells. Daudi cells incorporated approximately 3 times the radioactivity into the postmicrosomal supernatant than other cell types. Treatment with specific antisera to immunoglobulin showed that 3.3% of the incorporated radioactivity occurred in the bound polyribosomes and 0.4% in the free polyribosomes that precipitated as immunoglobulin; in the postribosomal supernatant 2.5% of the radioactivity was found in immunoglobulin. Label incorporation into total acid-precipitable molecules in the microsomes and cell sap was virtually linear throughout the labeling period; most of the label was found in the microsomes and after 90 min was contained in peaks having the mobility of heavy and light chains. Galactose and fucose addition occurred within the Golgi complex. The possibility that the carbohydrate moiety is incomplete or abnormal cannot be excluded.

- 2010 HAPTOGLOBIN (Hp) LEVEL OF BLOOD SERUM IN LEUKAEMIC PATIENTS. (E.) Gurda, M. (Med. Acad., Cracow, Poland). *Folia Haemat* 95(1):37-41, 1971.

Blood serum haptoglobin levels were determined for 175 patients with acute, chronic myelogenous or chronic lymphocytic leukemia. Normal haptoglobin values were 98-120 mg% (arithmetic mean); all leukemic patients had haptoglobin values significantly elevated over normal. Values for acute, chronic myelogenous and chronic lymphatic leukemia were 216.49, 191.67, and 200.00 mg%, respectively. The differences in haptoglobin values among the 3 types of leukemia were not statistically significant, and no significant differences could be found between haptoglobin values of patients of differing sex and age.

- 2011 IMMUNOGLOBULIN LEVELS IN CHRONIC LYMPHOCYTIC LEUKAEMIA. (E.) Scamps, R. A. (Repatriation Gen. Hosp., Concord, Australia), A. M. Streeter and B. J. O'Neill. *Med J Aust* 1(10):535-536, 1971.

Serum immunoglobulin levels were determined by the radial diffusion technique for 43 hospital patients with chronic lymphocytic leukemia and for 42 normal subjects. Estimation of the total serum gamma-globulin levels by standard paper electrophoresis showed a reduction in total gamma-globulin in only 37% of leukemia patients. Serum IgG levels of leukemia patients, however, showed a mean value of 795 mg/ml, significantly reduced from the normal mean of 1,205 mg/ml. The serum IgA levels in leukemia patients showed a mean of 140 mg/ml compared to the mean for normal of 215 mg/ml. The most marked reduction in leukemia patients was in IgM; leukemic patients showed mean values of 30 mg/ml, and normals showed means of 140 mg/ml. The reductions in serum immunoglobulin levels showed no obvious correlation with any feature of the disease or clinical treatment.

- 2012 TRANSPLANTATION OF BOVINE LYMPHOSARCOMA.
(E.) Donawick, W. J. (Sch. Vet. Med., U. Pennsylvania, Kennett Square), C. Johnstone, J. G. Martens, D. C. Dodd, J. E. Martin and R. R. Marshak. *Bibl Haemat* 36:493-499, 1970.

Calves were given injections of antilymphocyte serum (ALS) in amounts of 2 ml/kg s.c. every second day, beginning 13 days prior to the administration of cell suspensions of lymphosarcomas prepared from adult cows. Lymphosarcoma cells were transplanted to the vicinity of the prefemoral lymph nodes of the calves. In 10 of 14 primary passage attempts, progressively growing lymphosarcomas appeared in ALS-treated calves; 3 of 6 calves developed tumors in the first serial passage. Subsequent attempts to pass the tumor serially were fruitless. In calves in which ALS treatment was suspended 37 days after lymphosarcoma transplant because there was no evidence that the transplant had taken, enlarged peripheral lymph nodes and leukemic peripheral blood counts were observed after 2 wk. Lymphosarcoma developing in 4 calves was generalized; in other calves, lymphosarcomas had spread from the site of inoculation to the iliac lymph nodes. No tumors developed within 100 days after challenge with lymphosarcoma cells in untreated control calves or in calves given normal horse serum.

- 2013 IMMUNOFLUORESCENT STUDIES IN LYMPH NODES FROM CATTLE AFFECTED WITH BOVINE LEUKOSIS.
(E.) Trainin, Z. (Kimron Vetr. Inst., Bet Dagan, Israel) and U. Klopfer. *Bibl Haemat* 36:500-503, 1970.

Lymph nodes and spleens of leukotic cattle were examined by direct immunofluorescence staining with conjugated rabbit anti IgM bovine serum and conjugated rabbit anti-IgG bovine serum to determine whether these 2 proteins were present in spleens and lymph nodes of animals which lacked IgM in their blood. In neoplastic lymph nodes of cattle whose blood lacked IgM, and in those of 1 cow having IgM in the blood, no cells containing IgM were found. Normal lymph nodes and spleens of blood IgM-negative cows contained IgG but not IgM. There appears to be a connection between the disappearance of IgM from the blood of leukotic cattle and the absence of IgM from spleen and lymph nodes.

- 2014 ANTIGENICITY OF HUMAN CHORIOCARCINOMA.
(E.) Srivannaboon, S. (U. Michigan Med. Ctr., Ann Arbor). *Int J Fertil* 16(1):36-41, 1971.

Rabbits immunized in the foot pads with 1 ml of choriocarcinoma tumor cell homogenate emulsified in equal volumes of Freund's incomplete adjuvant were challenged 4 wk post-immunization on 3 consecutive days with i.v. injections of 0.4 ml of the tumor cell suspensions without adjuvant. Pooled rabbit antiserum was absorbed with normal hamster serum and placenta, normal human kidney and placenta, and human chorionic gonadotropin. Results of immunoelectrophoresis patterns obtained with unabsorbed and absorbed antisera showed a degree of cross-reactivity

between hamster placenta and human choriocarcinoma. A significant decrease in cell viability was seen following incubation of cells cultured *in vitro* and treated with the rabbit antiserum to human choriocarcinoma.

- 2015 CELLULAR IMMUNITY TO NEPHROBLASTOMA. (E.) Diehl, V. (Karolinska Hosp., Stockholm, Sweden), B. Jereb, J. Stjernswärd, C. O'Toole and L. Ahström. *Int J Cancer* 7(2):277-284, 1971.

Tumor-related cell-bound immunity to autochthonous and allogeneic nephroblastoma tumor cells was studied in human lymphocytes by means of micro-plate assay. Cytotoxic reduction by lymphocytes from healthy subjects and surgical patients was 27.8% for the tumor and 21.8% for normal tissue with corresponding figures for lymphocytes from patients with tumors other than nephroblastoma showing no significant difference at 32.3% and 48.2%, resp. In 10 out of 24 nephroblastomas, cytotoxic reduction by lymphocytes was significantly increased at $P < 0.01$, < 0.05 , and < 0.001 , and in 11 out of 26 micro-plate tests the reduction of tumor cells by test lymphocytes was significantly higher than that of control lymphocytes. No significant difference in the reactivity of 3 tumor tissues to cytotoxic lymphocytes was observed and in 26 micro-plate tests the specific cytotoxicity ranged between 22.3% and 35.8% when the allogeneic control cytotoxicity was taken as zero point. Lymphocytes from only 2 out of 8 patients with generalized disease had a stronger reaction on tumor tissue than those of control subjects, while lymphocytes from 8 out of 16 patients without dissemination of the disease reacted more strongly than those of control individuals. It is not known whether the present findings reflect true variation in tumor-related cytotoxic reactivity or whether the variation is due to a general decrease in immunologic reactivity with increasing tumor burden.

- 2016 HOST IMMUNE RESPONSE TO A COMMON CELL-SURFACE ANTIGEN IN HUMAN SARCOMAS: DETECTION BY CYTOTOXIC TESTS. (E.) Wood, W. C. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and D. L. Morton. *New Eng J Med* 284(11):569-572, 1971.

Host immune response to cell-surface antigen in human sarcomas was studied by means of microcytotoxicity testing. Cytotoxicity to an osteosarcoma cell line was revealed in 58 of 83 serum samples from patients with different histologic types of sarcomas. Immunization of sarcoma patients with autochthonous irradiated sarcoma cells induced an increase in titer of cytotoxic antibody. These results suggest the possibility of favorably altering the immune response of a sarcoma patient to his tumor.

2017 ANTIGENS OF HUMAN WART TISSUE. (E.)
 Pass, F. (Albert Einstein Coll. Med.,
 Bronx, N.Y.), R. Janis and D. M. Marcus.
Invest Derm 56(4):305-310, 1971.

Adult male rabbits were immunized with 10 mg inocu-
 lations of a homogenate prepared from human wart
 tissue, and sera were collected for immunological
 study. On indirect immunofluorescence tests,
 tissue from 5 human warts showed areas of nuclear
 and cell surface fluorescence; fluorescence was
 usually most conspicuous in the stratum granulosum.
 It was not possible to determine whether the cell
 surface fluorescence was due to the cell membrane
 or intercellular antigens. Rabbit antiserum did
 not produce a fluorescent reaction when reacted
 with normal human skin. A single band of
 precipitation was seen when the rabbit antisera
 were reacted with an aqueous extract of wart
 tissue in agarose gel diffusion. The rabbit
 antiserum showed nuclear and cell surface fluores-
 cence when reacted with keratoacanthomas and
 squamous cell carcinomas. No fluorescence was
 seen when antiserum was reacted with basal cell
 carcinoma tissue. Immunofluorescence and gel
 diffusion reactions were inhibited by absorption
 of rabbit antisera with large quantities of
 normal skin or tumor homogenates; however, the
 reactions were not inhibited by absorbing the
 antiserum with wart virus.

2018 IMMUNOLOGICAL STUDIES WITH HUMAN GLIOMAS.
 (E.) Mahaley, M.S., Jr. (Duke U. Med.
 Ctr., Durham, N.C.). *J Neurosurg* 34(3):458-459,
 1971.

The antigenic potential of human gliomas and the
 feasibility of producing heterologous antiglioma
 "carrier" antibodies capable of preferential glioma
 localization *in vivo* were studied utilizing fresh
 human glioma tissue homogenate for immunization of
 rabbits. In patients receiving radioantibody in the
 form of heterologous antiglioma globulin (125 I)
 infusion prior to a second operation, external brain
 scans revealed localization of the antibody within
 the area of the recurrent glioma. Upon direct
 inspection, localization within tumor tissue as
 compared with normal brain tissue was found in the
 majority of cases. To date, no proof of specific
 glioma antigens or specific antiglioma antibody
 production has been established.

2019 TONSILLECTOMY AND HODGKIN'S DISEASE: THE
 LYMPHOID TISSUE BARRIER. (E.) Vianna, N. J.
 New York St. Dept. Hlth., Albany, N. Y.), P. Greenwald
 and J. N. P. Davies. *Lancet* 1(7696):431-432, 1971.

Interviews were conducted with 109 patients with Hodg-
 kin's disease and 109 controls to determine whether
 the former group included an unusually large number of
 subjects who had undergone tonsillectomy. It was
 found that 67 Hodgkin's disease patients and 43 con-
 trols had undergone tonsillectomies. The estimated
 relative risk of developing Hodgkin's disease among

those with a history of prior tonsillectomy was 2.9
 times higher than that for those who had never been
 tonsillectomized. It was hypothesized that surgical
 removal of active lymphoid tissue in some way facili-
 tates the onset of Hodgkin's disease, perhaps by re-
 moving a protective barrier.

2020 MYELOMA PROTEINS IN A CASE OF MEDULLARY
 AND EXTRA-MEDULLARY SPREAD OF PLASMOCY-
 TOMA. (Ger.) Eulitz, M. (1st Med. Clin. U. Munich,
 Germany), D. Huhn and H. Eulitz. *Blut* 22(1):1-11,
 1971.

2021 A SEROLOGICAL STUDY OF THE IMMUNOLOGICAL
 BEHAVIOR OF CHILDREN'S NEOPLASMS. (Fr.)
 Nigro, N. (Pediat. Clin. U. Turin, Italy), G.
 Guarini, L. Benso, E. Madon, P. Iudicello and R. M.
 Jacob. *Presse Med* 79(6):227-228, 1971.

2022 THE EFFECT OF FREUND'S ADJUVANT ON THE
 GROWTH AND METASTASIS OF A TRANSPLANTABLE
 TUMOR OF THE CCK STRAIN. (Rus.) Volegov, A. I.
 (P. A. Herzen Inst. Oncol. Moscow, U.S.S.R.). *Pat*
Fiziol Eksp Ter 14(6):74-75, 1970.

2023 THE DISTRIBUTION OF HAPTOGLOBIN TYPES IN
 PATIENTS WITH LEUKAEMIA. (Ger.) Gurda,
 M. (Med. Acad. Cracow, Poland) and B. Turowska.
Folia Haemat 94(4):309-313, 1970.

See also:

- * (Rev): 1734, 1736, 1737, 1738, 1739, 1740, 1754,
 1758, 1760
- * (Chem): 1815
- * (Viral): 1880, 1927, 1929

- 2024 ENZYME HISTOCHEMISTRY AND AUTORADIOGRAPHIC STUDIES DURING DEVELOPMENT OF URINARY BLADDER TUMORS OF THE RAT. (Ger.) Kunze, E. (Path. Inst. U. Munich, Germany) and A. Schauer. *Z Krebsforsch* 75(2):146-160, 1971.

Hyperplasia of the urinary bladder mucosa followed the administration of dibutyl nitrosamine (20 mg/kg/day in drinking water) to female Wistar rats. The hyperplastic mucosa showed zero alkaline phosphatase activity, diminished NADPH-diaphorase and elevated succinic dehydrogenase. The hyperplastic areas developed 16 papillomas and 2 carcinomas, and these lesions also showed no alkaline phosphatase activity. The papillomas retained NADPH-diaphorase and succinic dehydrogenase at normal levels except in certain regions where the former enzyme was diminished and the latter was increased. In areas of zero alkaline phosphatase the ^3H -thymidine labeling index/100 cells had increased 41-fold over normal levels; the increase in the ^3H -thymidine labeling index was 105-fold in papillomas. Papillomas showed a 150% rise and enzyme-defective zones a 190% rise in grain density/surface unit values.

- 2025 TRANSFER RIBONUCLEIC ACIDS IN RAT LIVER AND MORRIS 5123 MINIMAL DEVIATION HEPATOMA. (E.) Gonano, F. (Inst. Gen. Path., U. Modena, Italy), V. P. Chiarugi, G. Pirro and M. Marini. *Biochemistry* 10(5):900-908, 1971.

Alterations in the chromatographic patterns of transfer ribonucleic acids obtained from rat liver and so-called "minimal deviation hepatoma" Morris 5123 were compared by reverse phase chromatography. Seventeen out of 20 amino acids showed the same profile for both rat liver and Morris 5123 hepatoma tRNA. Asparaginyl-tRNA was eluted from the Morris hepatoma at slightly higher salt concentrations in relatively different proportions; glutamyl-tRNA showed one peak of acceptor activity in the hepatoma compared to two in rat liver, whereas glutaminyl-tRNA showed a reverse profile. Phenylalanyl-tRNA differed also between the two tissues with respect to acceptor activity peaks and elution fractions. However, no significant differences were observed among the phenylalanyl-tRNAs from liver, Morris hepatoma and *E. coli* in their capacity to synthesize polyphenylalanine in response to polynucleotide template. In the tumor cell, the appearance of a new tRNA or the disappearance of a tRNA could influence the translation of some pre-existing mRNA into which amino acids have to be inserted.

- 2026 THE "STADE EPHELIDE" OF PRECANCEROUS MELANOSIS: A COMPARATIVE, CLINICAL, HISTOPATHOLOGICAL AND ELECTRON MICROSCOPICAL STUDY. (Ger.) Anton-Lamprecht, U. (U. Clin. Heidelberg, Germany), U. W. Schnyder and W. Tilgen. *Arch Derm Forsch* 240(1):61-78, 1971.

A case of "stade ephelide" arising in a 60-yr-old man presented the clinical features of a growing hyper-

pigmented facial freckle; histopathological evaluation of the freckle showed that the hyperpigmentation was confined to the basal and suprabasal cells of the epidermis. Under the electron microscope, the freckle - thought to be an early stage of cancerous melanosis - showed abundant malignant melanocytes in the basal cell layer. These melanocytes showed increased synthetic activity, and their melanin granules were similar to those seen in later stages of precancerous melanosis.

- 2027 PROLIFERATIVE CHANGES OF THE EPITHELIUM OF THE FALLOPIAN TUBE IN PATIENTS WITH ENDOMETRIAL CARCINOMA. (Ger.) Dallenbach-Hellweg, G. (Mannheim Clin., U. Heidelberg, Germany) and W. Rom. *Arch Gynaek* 209(4):396-410, 1971.

Non-invasive epithelial proliferation *in situ* was found in the fallopian tubes of 58 post-menopausal women with carcinoma of the endometrium. Fallopian tube epithelium also showed stratification, papillae and small alveolar spaces. The cytoplasm of the epithelial cells was rich in RNA, and their nuclei were large, pleomorphic, and rich in DNA. Therapy with estrogen had varying effects on fallopian tube hyperplasia and endometrial carcinoma. Patients aged from 60-70-yr-old showed the most extensive epithelial proliferation in their fallopian tubes. Estrogen stimulation was thought to be the cause of both the endometrial cancer and the hyperplasia of the fallopian tubes. In some cases, tubal hyperplasia had its onset prior to the onset of endometrial carcinoma, and in other cases the 2 conditions were initiated simultaneously.

- 2028 DARK CELLS IN THE EPITHELIAL TUMORS OF THE URINARY BLADDER. (Rus.) Romanenko, A. M. (Sci. Res. Inst. Urology, Kiev, U.S.S.R.). *Arkh Patol* 33(3):33-37, 1971.

Histological and histochemical investigations of the dark cells in 100 human bladder epithelial tumors (14 transitional cell papillomas, 28 well-differentiated, 32 moderately differentiated and 26 anaplastic tumors) revealed that the amount of dark cells increased with the progression of dedifferentiation. The polymorphism of the dark cells increased with the intensification of atypia of the light cells and was maximal with anaplastic tumors. An accumulation of nucleic acids, SH-groups and S-S bridges and a decrease in acid and neutral mucopolysaccharides was noticed with the progression of atypia. The histochemical features of the dark cells indicated that they were the most active epithelial elements within the tumor tissue and the rate of their occurrence appeared to correlate with increasing malignancy.

- 2029 BENIGN MAMMARY TUMORS AND CANCER DEVELOPMENT. (Ger.) Bussmann, J. F. (Mannheim Clin. U. Heidelberg, Germany), K. R. Loewe and H. S. Fürstenberg. *Bruns Beitr Klin Chir* 218(5):393-402, 1971.

Four hundred mammary benign tumors were classified as 205 chronic fibrosa cystica, 122 fibromatosis, and 73 fibroadenoma. The incidence of the development of malignancy from benign tumors was evaluated and compared to the normal population. Such development was often related to an increase in epithelial cell proliferation which was particularly marked in the cases of chronic fibrosa cystica, but was also found in the other types examined. Statistical evaluation was difficult since other factors, changes in the breast at the time of the menopause and malignancy attributable to ovulation inhibitors, often interfered with judgment of carcinogenesis. In one case where a mastectomy was not performed in the face of finding increased epithelial cell proliferation and atypical nuclei and which was diagnosed as fibrosa cystica, the patient developed a carcinoma in 10 yr; but in 2 patients with fibromatosis and increased epithelial cell proliferation and in whom mastectomy was not performed, no carcinoma had developed 8-10 yr later.

- 2030 PRECANCEROUS ALTERATIONS OF THE HUMAN THYROID. (Rus.) Zaridze, D. G. (Inst. Exp. and Clin. Oncol. Acad. Med. Sci. Moscow, U.S.S.R.) and N. T. Raykhlin. *Arkhl Patol* 33(3):16-22, 1971.

The pathogenic relationship between the nodular goiter, thyroid adenoma and thyroid cancer was investigated in preparations from 38 thyroid adenomas and 67 thyroid cancer patients. Epithelial proliferation of monomorphous cells with well-defined boundaries and oval nuclei towards the interfollicular spaces was the main feature observed in adenomas. A thickening of the follicular walls consisting of several cell layers was seen, often leading to the development of papillary structures with a well-defined connective stroma. Giant cells and a beginning of cell polymorphism with elongated and hyperchromic nuclei were seen in 7 of the adenomas and were suggestive of premalignant alterations. Adenomatous regions with considerable polymorphism of the epithelial cells surrounding the cancerous foci were observed in 32 of 67 cancer preparations.

- 2031 MALIGNANT DEGENERATION OF GASTRIC ULCER. (Fr.) Loussouarn, J. (no affil) and J. Turpin. *Concours Med* 93(6):859-869, 1971.

- 2032 CIRRHOSIS AND PRIMARY LIVER CANCER DEVELOPED FROM GIANT CELL HEPATITIS IN AN INFANT. (Hung.) Sandor, T. (Szeged U. Med. Sci., Hungary). *Orv Hetil* 112(9):498-500, 1971.

- 2033 THE EPITHELIAL ORIGIN OF THE MIXED TUMORS OF THE PAROTID GLAND. (It.) Gallippi, G. (Inst. Anat. Histol. Path., U. Messina, Italy), G. Carrozza and G. Vermiglio. *Arch Ital Anat Istol Pat* 43(4):221-259, 1970.

- 2034 VAGINAL CARCINOMA AND CONSTITUTION. (Ger.) Vahrson, H. (U. Women's Clin., Giessen, Germany). *Z Geburtsh Gynaek* 174(1):93-100, 1971.

- 2035 THE OCCURRENCE AND SIGNIFICANCE OF MYO-EPITHELIAL CELLS (MYOTHELIA) IN TUMORS. (Ger.) Hamperl, H. (Path. Inst. Bonn, Germany) and E. Lichtenberger. *Klin Wschr* 49(3):144-148, 1971.

See also:

- * (Rev): 1729, 1757
- * (Chem): 1808, 1814
- * (Phys): 1845

- 2036 LYMPHOSARCOMA IN INDIAN ZEBU CATTLE. (E.) Naik, S. N. (Cancer Res. Inst., Tata Mem. Ctr., Bombay, India), R. D. Dabholkar and H. P. Randelia. *Oncology* 25(1):72-78, 1971.

The epidemiological, clinical and histopathological findings of bovine lymphosarcoma are discussed on the basis of a survey of more than 79,000 male adult Indian cattle of seven different breeds and crossbreeds in India. Only one case of lymphosarcoma was detected in a Malvi bullock of about 9-10 yr of age; a clinical picture of debilitation was seen with pale mucous membranes and symmetrically enlarged regional lymph nodes accompanied by difficulty in breathing due to enlarged pharyngeal and mediastinal lymph nodes. The lymph nodes were soft, greyish to reddish in color and bulged from the surface when cut, revealing a loss of cortico-medullary architecture with proliferative and necrotic areas; the enlarged spleen weighed 1,705 g and had an irregular border with elevated areas on the surface. The animal presented an anemic blood picture ($RBC=3.34 \times 10^6/l/cm^3$) and lymphocytosis (73%, $12,191/cm^3$) with atypical lymphocytes containing double nuclei and vacuoles in the cytoplasm and large numbers of immature lymphocytes or lymphoblasts. The liver, kidney and lungs showed no evidence of disease. The ultimate proof of an association between leukemia in domestic animals and man will depend on careful epidemiological investigations and isolation of the causative agent.

- 2037 ASSOCIATION BETWEEN RAINFALL AND ESOPHAGEAL CANCER IN CHILE. (E.) Zaldivar, R. (U. Tennessee Coll. Med., Memphis) and H. Robinson. *Beitr Path* 142(4):403-406, 1971.

A negative correlation was found between rainfall and incidence of esophageal cancer in Chile. Incidence rates for this condition in 1962-1964 were maximal (e.g., 0.8-1.3 log cases of esophageal cancer) in low-rainfall areas of the country (e.g., 0.05-0.5 log total rainfall in 1964) and minimal (e.g., 0.05-0.4 log cases) in areas of heavy rainfall (e.g., 3.0-3.6 log total rainfall). It was noted that the areas of low rainfall and high esophageal cancer incidence were areas of highly alkaline soil conditions; however, the possibility of a connection between alkalinity of soil and esophageal cancer was not explored.

- 2038 PATTERN OF MALIGNANCY IN A PLACE IN WESTERN INDIA. (E.) Kirtane, J. S. (Med. Coll. Baroda, India), B. A. Sayed and V. P. Vaishnav. *Brit J Cancer* 24(4):670-672, 1970.

The incidence of cancer of various sites in a population from Baroda, India was investigated, and it was found that of 4500 cases of malignancy, 25% involved cancer of the buccopharynx and 27.8% involved the female genital tract. Buccopharyngeal cancer affected more men than women, and accounted for 39.5% of all malignancies in men and for 4.8% of all malignancies in women. Most female genital tract cancer involved the cervix. Esophageal cancer was the most commonly

affected site in the gastrointestinal tract. Most cancers observed were epithelial in origin; sarcomas comprised only 6.2% of the observed malignancies. The high rate of buccopharyngeal cancer in men and its low rate in women may be due to the habit of chewing a mixture of tobacco and lime which is widespread among men in this area of India.

- 2039 THE EPIDEMIOLOGY OF CANINE LEUKEMIA AND LYMPHOMA. (E.) Dorn, C. R. (Sch. Vetr. Med., U. Missouri, Columbia), D. O. Taylor and R. Schneider. *Bibl Haemat* 36:403-415, 1970.

A survey of the occurrence of leukemia and lymphoma among dogs in Alameda County, California revealed that the average annual incidence rate for lymphosarcoma and reticulosarcoma for dogs (24.2 cases/1000,000 population) was higher than the rate for men (4.7 cases/100,000) and lower than the rate for cats (128.4/100,000). No evidence of spatial or temporal clustering could be found for leukemia or lymphoma in dogs, nor did the incidence of these conditions exhibit any seasonal pattern. About 89% of leukemia-lymphoma diagnoses among dogs in Alameda county were lymphosarcomas, and the incidence rate for lymphosarcomas among dogs increased with age of the dog up to 11 yr-of-age, the period of peak incidence (84.03/100,000). Male and female dogs appeared to have comparable risks for developing lymphosarcoma. Age-specific incidence rates for lymphosarcoma among dogs were lower than the rates for mastocytoma and fibrosarcoma, and higher than rates for hemangiosarcoma and osteosarcoma. Of 8 breeds of dogs examined, only the boxer had a significantly greater number of lymphosarcoma cases than expected, the risk of lymphosarcoma development among boxers being 9.5 times higher than the risk among all other dogs combined. Boston terriers were found to be at an unusually high risk for malignant mastocytoma and hemangiosarcoma. No pattern of multiple occurrence of primary malignancies was seen, although sarcomas and lymphomas were seen to occur in the same dog.

- 2040 SOME LESSONS FROM CANCER PATTERNS IN AFRICA. (E.) Burkitt, D. P. (Med. Res. Council, London, England). *Med Proc* 17(4-5):52-58, 70-74, 1971.

Incidence of cancer of various sites in various regions of Kenya and Tanzania was investigated. Esophageal cancer was more rare in western Kenya and Tanzania than in the central and eastern regions of those countries and most prevalent in the vicinity of Lake Victoria. Kaposi's sarcoma was more common in the western parts of Kenya than in the east, as was carcinoma of the penis. Malignant lesions of the breast were more common in areas where benign lesions were widespread, and cancer of the colon was associated with appendicitis, diverticular disease, and adenomatous polyps. The rarity of bronchial carcinoma in Africa seemed to be related to the fact that relatively few Africans smoke cigarettes. The inverse relationship discovered between age at first pregnancy and liability of developing breast cancer

probably accounted for the low incidence of this condition in Africa. Cancer of the penis had a high incidence in parts of Africa where male circumcision was not the rule. Burkitt's lymphoma was especially prevalent in areas in which there was a high incidence of malaria, suggesting an insect vector for Burkitt's lymphoma. The use of tin-coated metal drums for the distillation of spirits and the use of maize beverages have both been suggested as etiological factors in the development of esophageal cancer in Africa.

2041 CANCER SURVEY IN SOUTH IRAN WITH SPECIAL REFERENCE TO GASTROINTESTINAL NEOPLASMS.

(E.) Barekat, A. A. (Pahlavi U. Sch. Med., Shiraz, Iran), F. Saidi and W. Dutz. *Int J Cancer* 7(2):353-358, 1971.

A survey of 1,987 male and 1,288 female cancer cases from the Fars Province of Iran was carried out to determine the relative frequencies of cancers of various sites in that region. The predominant malignant condition among males in the Fars Province was skin cancer, accounting for 19% of cancer cases. In Iran generally, skin cancer accounted for 26% of all cancers, while in Sweden it accounted for only 5% of all cancers. Cancer of the lymphoid system was the next most frequent malignancy in the area, comprising 12.4% of cancer cases, a proportion comparable to the proportion of all of lymphoid cancer cases in Iran generally and in Sweden. Cancer of the hematopoietic system was more prevalent in the Fars Province (5.6% of all cancers) than in Iran generally (0.4% of all cases). The most common cancer among females in the Fars Province was skin cancer and the next most prominent was cervical cancer, with incidences of 15.6 and 13.5% of all cancers, resp. While the prevalence of cervical cancer was similar in the Fars Province and in Sweden, breast cancer was more frequent in Sweden. Breast cancer, the third most prominent cancer among Fars Province females, was far less prevalent in Fars than in Sweden. While the frequency of esophageal cancer was relatively high, there was a dearth of cancer of the colon in Fars Province. Twenty-five percent of all lymphomas (18.1% and 11.2% in males and females, resp.) occurred primarily in the gastrointestinal tract.

2042 ASSESSMENT OF RISK PATTERNS IN CANCER OF THE CERVIX: A COMPARISON BETWEEN GREATER BOMBAY AND WESTERN COUNTRIES. (E.) Jussawalla, D. J. (Bombay Cancer Registry, India), V. A. Deshpande and J. Standfast. *Int J Cancer* 7(2):259-268, 1971.

A survey of 503 Bombay women with cervical cancer, was found that patients with cancer of the uterine cervix appeared to have married at an earlier age than women without cervical cancer; 60% of cancer patients had married before age 15 as against 37% of healthy controls. Six percent of the cancer patients became pregnant for the first time before age 15, compared to 1.1% for women without cervical cancer; furthermore, the risk of developing cancer of the uterine cervix was found to be 14 times higher in

women who had become pregnant for the first time before age 15 than it was in nulliparous women. Risk of developing cervical cancer increased in direct proportion to the number of pregnancies and was significantly higher in women who had undergone 3 or more pregnancies than in nulliparous women. Elapsed time between pregnancies was also correlated with risk of cervical cancer; women undergoing pregnancies in quick succession had a higher risk than women spacing their pregnancies.

2043 CANCERS OF THE LUNG AND NASAL SINUSES IN NICKEL WORKERS. (E.) Doll, R. (Dept. Regius Prof. Med., U. Oxford, England), L. G. Morgan and F. E. Speizer. *Brit J Cancer* 24(4):623-630, 1970.

A survey was conducted on 845 workers in a nickel refining installation in South Wales to determine whether this population had an unusually high mortality rate from lung and nasal carcinoma. The 845 workers had been employed at the nickel plant for at least 5 yr and in all cases, their employment had commenced before 1944. Men starting employment before 1925 had a mortality from nasal cancer varying from 100-900 times that in Britain at large; in this group the expected number of nasal cancer deaths was 0.107 and the observed number was 39. No deaths from nasal sinus cancer were seen in men who started work in the nickel plant in 1925 or later, by which time the carcinogenic nickel carbonyl had been eliminated from nickel plants. The observed mortality from lung cancer in nickel workers commencing work before 1925 was 5-10 times that expected in the nation at large. Mortality from other cancers was also slightly elevated among nickel workers employed before 1925, observed and expected deaths from other neoplasms in this group being 49 and 31.5, resp. Mortality from causes other than cancer was about 20% above that predicted for all England and Wales in the pre-1925 nickel workers. It was found that susceptibility to induction of nasal cancer increased with age at first employment in the nickel plant, and that risk remained approximately constant for 15-42 yr after the carcinogen had been removed from the workers' environment. Susceptibility to induction of lung cancer, on the other hand, did not increase with age at first exposure to the nickel plant environment, and risks for lung cancer varied irregularly. The risk of lung cancer development declined after removal of the carcinogen from the environment; the earlier high mortality may have eliminated nickel workers who were heavy cigarette smokers from the study population.

2044 EPIDEMIOLOGY OF FELINE LEUKEMIA (LYMPHOSARCOMA). (E.) Brodey, R. S. (U. Pennsylvania Sch. Vetr. Med., Philadelphia), S. K. McDonough, F. L. Frye and W. D. Hardy. *Bibl Haemat* 36:333-342, 1970.

The incidence of feline lymphosarcoma (LSA) was investigated in 64 cats residing in 15 household "clusters." Thirty-eight cases of LSA were surveyed in this population. Ten of the household clusters contained 2 cats, 3 contained 3 cats, 1 contained 4 cats

and 1 contained 5 cats. The proportions of affected cats to the number of cats in the cluster ranged from 2/7 to 3/3, and the interval between deaths of cats from LSA in a single cluster ranged from 2-33 months. Most LSA lesions were multicentric; however, favored single sites were the alimentary system and the mediastinum. Only 2 of the 38 affected cats were related, suggesting that transmission of LSA among cats in a cluster was horizontal, perhaps proceeding *via* the transmission of virus in saliva. In several of the clusters, cats moved between households, a factor which appeared to be important in the transmission of LSA in these clusters.

- 2045 PREVALENCE AND INCIDENCE RATES OF CERVICAL ATYPIA: A COMPUTERIZED FILE ANALYSIS ON 148,735 PATIENTS. (E.) Bibbo, M. (Dept. Obstet. Gynec. U. Chicago, Ill.), C. M. Keebler and G. L. Wied. *J Repr Med* 6(4):184-188, 1971.

A computerized survey of 148,735 patients undergoing screening for cervical atypia over a 10-yr period showed that dysplasia was most common in women 25-29-yr-old (1,036 cases), carcinoma *in situ* was most common in women 25-29-yr-old (244 cases), and invasive carcinoma was most common in women 49-yr-old or over (111 cases). The lowest rate of prevalence of cervical dysplasia was found among women 49-yr-old or over. Prevalence rates for cervical lesions were calculated for pregnant women, currently non-pregnant women, current oral contraceptive users, current IUD users and women who used neither oral contraceptives nor IUD's prior to their first cervical examination. Current IUD users had the highest prevalence rates for cervical dysplasia among the 6 groups, and women using neither IUD's nor oral contraceptives had the lowest prevalence rates for dysplasia. Current oral contraceptive users and current IUD users had higher prevalence rates for carcinoma *in situ* than other selected groups. Women currently not pregnant and women using neither IUD's nor oral contraceptives had higher rates of invasive squamous cell carcinoma than other groups; pregnant women had the lowest rate of invasive cancer.

- 2046 EPIDEMIOLOGY OF MESOTHELIOMA ON WALCHEREN ISLAND. (E.) Stumphius, J. (Vlissingen, The Netherlands). *Brit J Indust Med* 28(1):59-66, 1971.

Of 277 shipyard workers from Walcheren Island (Netherlands) who had no history of acute or continuous exposure to asbestos dust, 160 (57.8%) showed asbestos dust bodies in sputum samples. Among workers with no exposure to asbestos dust, the percentage of positive sputum samples was 39.4%, while among those with histories of exposure to iron vapor, rust and "some" asbestos dust, percentages of positive sputum samples ranged from 70-100%. Many of the workers currently employed in occupations not exposed to asbestos dust who had asbestos bodies in their sputum had been exposed to asbestos dust 5-10 yr prior to the time of the experiment. Of 25 cases of mesothelioma recorded on Walcheren Island between 1962-1968,

22 had been employed in the shipbuilding industry at some time, and all but 3 of these workers had been exposed to asbestos dust sometime in the course of their employment in the shipyards. The incidence of mesothelioma in the shipyard population was about 100 cases/100,000 males/yr, while the incidence rate for Dutch provinces with heavy industry was 1 case/100,000 males/yr. Incidence of mesothelioma among workers in the shipyards with no asbestos exposure and among workers with "some" asbestos dust exposure were 50 and 280 cases/100,000 males/yr, resp.

- 2047 BREAST CANCER ANOMALIES. (E.) Stocks, P. (Colwyn Bay, North Wales). *Brit J Cancer* 24(4):633-643, 1970.

Death rates from breast cancer among women under 45 yr of age in England and Wales decreased between 1951-1959, then rose during 1960-1969 from 121 deaths/10⁶ population in 1959-1963 among women 25-44-yr-old to 136 deaths/10⁶ population in 1964-1967 in the same age group. Breast cancer death rates were lower in the north of England and in Wales than in southern England, with 600 deaths/10⁶ population occurring among women aged 45-64 in the Northern Counties in 1959-1963 and 783 deaths/10⁶ population occurring in the same age group in "greater London". After 1958 the excess of breast cancer deaths in southern England among women under 45-yr-old disappeared. The reasons for the increase in breast cancer death rates since 1960, and for the lower mortality in the north are unknown. An inverse relationship was seen between incidence of breast cancer and incidence of uterine cancer in northern and southern England; the breast cancer: uterine cancer death rates ratio among women in the Northern Counties aged 45-64-yr-old in 1959-1963 was 1.98 while the ratio for the same age group at the same time in greater London was 3.18. Total mortality from breast and uterine cancer combined, however, has shown little regional variation. The northern regions having low breast cancer rates were found to be regions where the consumption of liquid milk was low; high breast cancer rates (e.g., in London) were found to be correlated with high milk consumption. Similar correlations were found for breast cancer incidence and per person intake of butter, cheese and green vegetables, suggesting a causal connection between breast cancer mortality and the consumption of these foods.

- 2048 COMPARATIVE STUDY ON GEOGRAPHICAL DISTRIBUTION OF HUMAN AND CATTLE LEUKOSIS (E.) Khokhlova, M. P. (Min. Publ. Hlth., USSR, Moscow) and P. P. Rakhmanin. *Bibl Haemat* 36:654-658, 1970.

High mortality rates from leukosis and other lymphoid and hematopoietic malignancies were found to occur in Lithuania, Latvia and Estonia, areas where the incidence rate of leukosis among cattle is also high. In Latvia, areas where the mortality among humans from leukosis was below 7 cases/100,000 population were areas where the mortality among cattle from leukosis was below 20 cases/100,000 head of cattle;

areas where the mortality among humans from leukosis was above 10 cases/100,000 were areas where the mortality from leukosis among cattle was above 100 cases/100,000. Cases of human leukosis occurring in narrowly localized areas (e.g., one farm or adjacent farms) were often recorded from areas with a high prevalence of leukosis in cattle herds.

- 2049 DEATHS FROM LUNG CANCER IN AUSTRALIA. (E.) McCall, M. G. (Dept. Med., U. Western Australia, Perth) and N. S. Stenhouse. *Med J Aust* 1(10):524-525, 1971.

Deaths from lung cancer in Australia recorded between 1962-1966 were surveyed to examine mortality from this condition among various immigrant groups in Australia. The death rate for native-born Australians from cancer of the lung was found to be significantly lower than the death rate for immigrants from England, Wales and Scotland. Among persons 40-49-yr-old, there were 16 deaths/100,000 population among the native-born, 28 among English and Welsh immigrants, and 44 among Scots immigrants. The mortality from lung cancer among immigrants to Australia was lower than the mortality among native-born Scots, Englishmen and Welshmen who remained in their homelands. Among immigrants to Australia, age at date of immigration was correlated with lung cancer mortality; those immigrating at an average age of less than 25-yr appeared to show a subsequent lung cancer rate similar to the rate for native-born Australians, while those immigrating to Australia at a more advanced age had increased risks of developing lung cancer. The results were thought to indicate that air pollution played an important role in the genesis of lung cancer in the immigrant groups.

- 2050 A PRELIMINARY REPORT ON THE THYMIDINE LABELING INDICES AND KINETICS OF CELL PROLIFERATION IN SELECTED MORRIS HEPATOMAS. (E.) Looney, W. B. (U. Virginia Sch. Med., Charlottesville), A. A. Mayo, M. Y. Janners, J. G. Mellon, P. Allen, D. Salak and H. P. Morris. *Brit J Cancer* 24(4):826-832, 1970.

Kinetics of cell proliferation and cell loss in Morris hepatomas (H-35tc₂, R-7, 7797, 9611B and 8999) were studied in ACI strain female rats by means of thymidine labeling. The 1 hr thymidine labeling index for the hepatomas ranged from 3.3 to 13.9 and chromosome numbers showed no correlation with the labeling index. The per cent of labeled cells in hepatomas was greater than is found in normal liver before the onset of DNA synthesis and less than the 19.1% at the peak of DNA synthesis in regenerating liver.

- 2051 THE KINETICS OF CELLULAR PROLIFERATION IN NORMAL AND MALIGNANT TISSUES: A REVIEW OF METHODOLOGY AND THE ANALYSIS OF CELL POPULATION KINETICS IN HUMAN TISSUES. (E.) Fabrikant, J. I. (U. Connecticut Sch. Med., Farmington). *Amer J Roentgen* 111(4): 700-711, 1971.

Kinetic parameters of cellular proliferation were ascertained in normal, neoplastic and inflammatory

tissues of the larynx and adjacent tissues from more than 200 patients. Neoplastic tissues included benign squamous cell papillomas of the larynx and malignant squamous cell carcinoma of the larynx. Sites of cell proliferation were determined by monitoring incorporation of tritiated thymidine in cells. In normal tissues, the label was uniformly distributed among zones of proliferation, while in inflammatory tissues, higher labeling indices were found in areas of acute inflammatory cell infiltration. In neoplasms, labeled cells appeared in clusters at different sites. The rate of cell proliferation varied widely in different tissue samples; however, the variation for tumors was comparable to that for normal tissues, and frequently less than that for inflammatory lesions. The duration of the DNA synthesis period (i.e., the duration of the S phase in mitosis) was greater in malignant than in benign tumor cells and was at a minimum in normal cells.

- 2052 BIRTH, DEATH AND NET GROWTH OF NORMAL TRANSFORMING, NEOPLASTIC AND MALIGNANT CELL LINES: DECREASE OF DEATH RATE IN NEOPLASTIC ALTERATION. (E.) Norrby, K. (Dept. I, Path., U. Göteborg, Sweden) and J. Mellgren. *Path Europ* 6(1):56-74, 1971.

Growth kinetics of cell populations were observed in normal and neoplastic human and animal cell cultures; material included fetal normal and juvenile normal human fibroblast-like cell lines from skin and lung, normal fetal cell lines transformed by SV40, an established tumor line derived from an osteogenic sarcoma in a 15-yr-old girl, normal hamster embryo fibroblasts, and spontaneous and SV40-induced hamster sarcomas. Birth and death of cells in the cultures were observed and measured by means of a cinemicrographic technique. The "death index" of cells was expressed as a percentage of the effective birth rate of cells. It was found that the death index of human normal fetal and juvenile cells was 17-19%, while that for human virus-transformed cells and human juvenile neoplastic cells was about 7%. Death indices for normal and neoplastic cells were 27% and 6%, resp. Initially during the process of cell transformation, both birth and death rates of cells rose; this stage was followed by a period of fluctuating death rates in transformed cultures, which was in turn followed by a period of low cell death rate.

- 2053 CANCER: DISEASE AND MORTALITY. (Ger.) Wagner, G. (German Cancer Res. Inst., Heidelberg, Germany). *Therapiewoche* 21(9):644-651, 1971.

- 2054 DESCRIPTIVE STATISTICS ON A NINE-YEAR SURGICO-PATHOLOGICAL SERIES FROM A KOREAN POPULATION: WITH PARTICULAR REFERENCE TO MALIGNANT TUMORS. (E.) Wetteland, P. (Natl. Med. Ctr., Seoul, Korea). *Acta Chir Scand* (Supp. 412):1-66, 1970.

- 2055 THE SOCIAL ASPECT OF MALIGNANT TUMORS IN CHILDHOOD. (It.) Lucca, A. (Turin, Italy) and R. Morbidelli. *Med Soc* 20(10):366-376, 1970.

See also:

- * (Rev): 1732, 1741
- * (Chem): 1782, 1834
- * (Phys): 1854
- * (Immun): 2005

- 2056 N-ACETYLATION OF ARGININE-RICH HEPATOMA HISTONES. (E.) Byvoet, P. (Div. Biol. Sci., U. Florida, Gainesville) and H. P. Morris. *Cancer Res* 31(4):468-470, 1971.

Rats with hepatomas and normal rats were given i.p. injections of 100 μ C 14 C-L-alanine/kg to label liver cell histones and 2 mC/kg 3 H-sodium acetate to label histone N-acetyl groups. Decay rates of the N-acetyl groups in the combined arginine and slightly lysine-rich histones from normal and neoplastic tissues were observed. The $t_{1/2}$ in hr for the histone N-acetyl group turnover in Morris hepatoma 3924A and normal liver of Buffalo rats was 1.5 and 1.9, resp. In Novikoff hepatoma cells the $t_{1/2}$ of the histone N-acetyl group was 21 hr; the $t_{1/2}$ for L-alanine- 14 C-labeled histones was 41 hr. The latter figure was similar to the values obtained for L-alanine- 14 C-labeled histones in all normal and neoplastic tissues. In general, the N-acetyl groups turned over much more rapidly than whole histones or DNA, differences between N-acetyl group half-lives and whole histone group half-lives in Morris hepatoma cells often approaching a factor of 10.

- 2057 CHANGES IN PHOSPHOLIPID METABOLISM OF A TUMOR TARGET CELL DURING A CELL-MEDIATED CYTOTOXIC REACTION. (E.) Koren, H. S. (Max Planck Inst. Immunobiol., Freiburg, Germany), E. Ferber and H. Fischer. *Biochim Biophys Acta* 231(3):520-526, 1971.

C57Bl mice were given i.p. injections of 3×10^7 viable DBA/2 ascites mastocytoma cells; 10-11 days thereafter, the spleens of these mice were extracted and lymphocytes were prepared from them for incubation with mastocytoma cells. Phospholipid metabolism in mastocytoma cells treated with spleen lymphocytes of immunized and unimmunized mice was observed by incubating tumor cells with 14 C-labeled oleic acid and lysolecithin. Mastocytoma cells alone incorporated label into membrane lecithin to the extent of 70% and 18% into neutral lipids. Normal lymphocytes caused a decrease in lecithin labeling in mastocytoma cells, and immune lymphocytes caused a 2-3-fold decrease. The degradation of lecithin in cultures of mastocytoma cells incubated with immune lymphocytes proceeded at a more rapid rate than did lecithin degradation in untreated mastocytoma cells or in mastocytoma cells treated with normal lymphocytes.

- 2058 BIOCHEMICAL CHANGES OF THE LIPID IN BIOPSIED LIVERS OF PATIENTS WITH MALIGNANT NEOPLASTIC DISEASES. (E.) Nakazawa, I. (Tohoku U. Sch. Med., Sendai, Japan) and S. Yamagata. *Tohoku J Exp Med* 103(2):129-139, 1971.

Human liver biopsies of 19 patients with malignant neoplastic disease, 26 patients with benign hepatic disease, 2 patients with benign hepatic disease with gastric cancer and 14 controls were subjected to histological examination and lipid analysis by means of thin layer chromatography and gas liquid chromatography. Results revealed a higher content of $C_{20:4}$ and lower $C_{14:0}$ and $C_{18:1}$ fractions in livers of patients with

malignancies compared to controls, while the group with benign hepatic disease showed an increase in the percentage of $C_{14:0}$, $C_{16:1}$ and $C_{18:1}$ and a decrease in percentage of $C_{18:0}$, $C_{18:2}$, $C_{20:4}$, and $C_{22:5}$. In the phospholipid fraction, a significant decrease in the percentage of $C_{14:0}$ was noted in malignant cases, and in 7 cases of benign hepatic disease no significant difference was noted in the percentage of fatty acids compared with the control group. In 7 cases of benign hepatic disease a significant decrease was recognized in the percentage of $C_{18:2}$ while values obtained from the malignant cases were similar to the control group. Content of the fatty acid in the phospholipid fraction of the human liver revealed a mean value of 15.08 mg/g liver in malignant cases compared with the mean value in 11 non-malignant cases of 12.24 mg/g liver and in 9 cases of benign hepatic disease 10.43 mg/g liver. The fatty acid content in the triglyceride fraction gave a mean value of 5.05 mg/g liver for 19 malignant cases compared with the mean of 8.07 mg/g liver for 11 non-malignant cases and 6.76 mg/g liver for 9 cases with benign hepatic diseases.

- 2059 HYDROCORTISONE: INHIBITION OF DNA SYNTHESIS AND MITOTIC RATE AFTER LOCAL APPLICATION TO MOUSE EPIDERMIS. (E.) Hennings, H. (U. Wisconsin Med. Ctr., Madison) and K. Elgjo. *Virchow Arch Zellpath* 8(1):42-49, 1971.

Female hairless mice were given topical doses of 10, 50, 100 or 250 μ g hydrocortisone on the dorsal epidermis; 1-48 days later, mice were given i.p. injections of 3 H-thymidine and 30 minutes before sacrifice, the incorporation of the 3 H label into epidermal cells was examined to determine the effect of hydrocortisone treatment on DNA synthesis. The highest dose of hydrocortisone inhibited DNA synthesis by more than 40% at all times tested between 4 and 24 hr; the inhibition of DNA synthesis produced by smaller doses of hydrocortisone was more gradual in onset, and animals given smaller doses of hydrocortisone recovered normal rates of DNA synthesis sooner than animals given 250 μ g of hydrocortisone. By 48 hr after hydrocortisone treatment, DNA synthesis had recovered in all animals. At all doses of hydrocortisone tested, the maximal inhibition of DNA synthesis was observed 12 hr after treatment. The inhibitory effect of hydrocortisone was not affected by the time of day at which the compound was administered. Inhibition of DNA synthesis by hydrocortisone was accompanied by a decrease in mitotic activity, indicating that cells in the G1 and G2 phase of mitosis were susceptible to the inhibitory effects of hydrocortisone. When epidermal chalone was used to treat mouse skin in addition to hydrocortisone it was found that the former agent did not affect the inhibitory effect of hydrocortisone. When croton oil was applied to mouse skin following hydrocortisone, the increase in DNA synthesis usually seen with croton oil was reduced.

- 2060 INTRACELLULAR HYDROGEN TRANSPORT SYSTEMS IN ACUTE LEUKAEMIA. (E.) Stuart, J. (Child Hosp., Birmingham, England), J. S. Simpson and J. R. Mann. *Brit J Haemat* 19(6):739-748, 1971.

Bone marrow smears from 10 children in the acute or remission state of acute lymphoblastic leukemia and 10 children with no known disease were incubated at 37° for 90 min in freshly prepared incubation solution containing nitroblue tetrazolium, fixed for 10 min in a 40% formalin solution following incubation, counterstained for 10 min with aqueous methyl green, and studied by means of a scanning and integrating microdensitometer set at the wavelength of green light. Marrow enzyme scores for small lymphocytes for 10 patients in hematological remission were not significantly different from controls with the exception of glucose-6-phosphate dehydrogenase which showed a significantly higher activity in the non-leukemic patients. The mean enzyme scores for blast cells of 24 children newly diagnosed or in relapse showed a significant increase in extramitochondrial lactate dehydrogenase, malate dehydrogenase and 3-hydroxybutyrate dehydrogenase with no significant increase in the activity of intramitochondrial respiratory dehydrogenases. Exposure to hyperbaric oxygen prior to incubation resulted in no significant alteration in dehydrogenase activity. The net transhydrogenation effect was significantly greater for both the blast cells of leukemic patients and PHA-transformed lymphocytes from normal adults compared with the small lymphocytes.

2061 CYTOPLASMIC AND NUCLEAR GLYCOGEN SYNTHESIS IN NOVIKOFF ASCITES HEPATOMA CELLS. (E.) Karasaki, S. (Hosp. Notre-Dame, Montreal, Quebec, Canada). *J Ultrastruct Res* 35(1-2):181-196, 1971.

Novikoff ascites hepatoma cells from transplanted tumors in rats were incubated with ³H-labeled D-glucose, and on electron microscope examination were found to have incorporated the label in β-type glycogen particles in the cell cytoplasm. Three minutes after incubation with labeled D-glucose, autoradiography showed that the label was localized mainly in glycogen foci which themselves showed no marked alteration from their normal state. Treatment of incubated cells with α-amylase resulted in an almost complete extraction of glycogen particles. Between 5-15 min after incubation of ascites cells with labeled D-glucose a significant growth of the glycogen area occurred in cell cytoplasm, accompanied by labeling of the newly formed glycogen particles. The number of α-type glycogen particles was seen to have increased. By 30-60 min after incubation, the size and number of glycogen particles had increased to maximum values; in 1 case a single glycogen island occupied more than half of the cytoplasm in the cell. The number of α-type glycogen particles and the number of intranuclear glycogen particles also increased by 60 min after incubation. By 120 min after incubation with labeled D-glucose, the size and number of glycogen foci in tumor cells had begun to decline.

2062 CHANGES IN HYBRIDIZABLE NUCLEAR RNA DURING THE NEOPLASTIC DEVELOPMENT OF MOUSE MAMMARY CELLS. (E.) Turkington, R. W. (Duke U. Med. Ctr., Durham, N. C.). *Cancer Res* 31(4):427-432, 1971.

Normal mammary glands, hyperplastic alveolar nodule outgrowths derived from primary nodules, spontaneous mammary carcinomas and serially transplanted mammary carcinomas of C3H/HeJ female mice were used to prepare nuclear tritium-labeled RNA and DNA which were compared by techniques of RNA-DNA hybridization and hybridization competition. The direct hybridization reaction did not detect differences in the RNA populations derived from hyperplastic alveolar nodule outgrowths or spontaneous carcinomas. Mammary gland RNA competed incompletely with hyperplastic alveolar nodule RNA, and spontaneous carcinoma RNA; hyperplastic alveolar nodule RNA competed incompletely with RNA from spontaneous carcinomas; RNA from the spontaneous carcinomas competed incompletely with RNA from the transplanted carcinomas demonstrating that successive stages of neoplastic development are characterized by a discreet increment in the diversity of hybridizable nuclear RNA species formed.

2063 ¹³¹I-LABELED COLLOIDAL HUMAN SERUM ALBUMIN IN THE STUDY OF RETICULOENDOTHELIAL SYSTEM FUNCTION: III. PHAGOCYTOSIS AND CATABOLISM COMPARED IN NORMAL, LEUKEMIC AND IMMUNOSUPPRESSED HUMAN SUBJECTS. (E.) Palmer, D. L. (U. Colorado Med. Ctr., Denver), D. Rifkind and D. W. Brown. *J Infect Dis* 123(5):465-469, 1971.

Eight immunosuppressed patients with recent renal homograft transplantations receiving large doses of azathioprine and prednisone with sustained renal functions and no evidence of hepatic or cardiovascular decompensation (6 males and 2 females, 16-45 yr) and 5 leukemia patients (4 females and 1 male, 48-68 yr) were injected i.v. with human serum albumin labeled with ¹³¹I to measure phagocytosis; its rate of appearance in the blood was used to measure the catabolism of the colloid. Both the leukemic and transplant patients had significantly greater amounts of slowly phagocytized labeled human serum albumin than the normal patients; there was no relationship between the chronic and acute type of leukemia or duration of the disease and the rate of phagocytosis. The duration of the lag phase varied between 0 and 16.0 min for all patients with no significant difference noted among the groups; however, catabolic breakdown was significantly more rapid for the leukemic patients compared to the other groups with a value of 318 min for the leukemic group and 686 min and 573 min for the normal and transplant patients, resp. The initial phagocytic rate, the rate of catabolism and the amount of material not rapidly cleared appeared to be independent of each other.

2064 TYROSINE HYDROXYLASE IN NEUROBLASTOMA. (E.) Imashuku, S. (Kyoto Prefect. U. Med., Japan), E. H. Labrosse, E. M. Johnson, Jr., V. H. Morgenroth, III and N. Zenker. *Biochem Med* 5(1):22-29, 1971.

Two neuroblastomas excised from Negro children were assayed for tyrosine hydroxylase activity; tyrosine hydroxylase in the tumor tissues was found to require tetrahydropyridine (DMPH₄). Tyrosine hydroxylase

activity, measured in nmoles/25 mg/10 min of dopa formed, was zero in the absence of DMPH₄ in both tumors, and 0.874 and 0.183 in the 2 tumors in the presence of DMPH₄. Ferrous ion enhanced the level of tyrosine hydroxylase activity in the presence of DMPH₄; enzyme values for the 2 tumors in the presence of DMPH₄ and Fe²⁺ were 1.46 and 0.681, resp. Catecholamines and other inhibitors, including L-dopa, dopamine, DL-norepinephrine, DL- α -methyl-tyrosine, and benzimidazole-5(6)-DL-alanine dihydrochloride inhibited tyrosine hydroxylase activity in the neuroblastomas to the same extent as they inhibited the enzyme in bovine adrenal tissue, suggesting that neuroblastoma tyrosine hydroxylase was normally susceptible to feedback inhibition.

2065 CONTROL MECHANISMS OF ADENINE NUCLEOTIDE METABOLISM OF ASCITES TUMOR CELLS. (E.)

Yushok, W. D. (Inst. Cancer Res., Fox Chase, Philadelphia, Pa.). *J Biol Chem* 246(6):1607-1617, 1971.

Changes in the adenine nucleotide quotient [(ATP)(AMP)/(ADP)²] of Ehrlich ascites cells grown in female white Swiss mice of the ICR strain in response to adenosine, inosine, L-glutamine, and inorganic phosphate were studied. Aerobic incubation with adenosine and inosine increased the ATP, AMP and total adenine nucleotide content; added adenosine doubled the adenine nucleotide within 60 min. Glucose in combination with L-glutamine increased the adenine nucleotide by 0.5 μ mole/ml of cells in 30 min in the presence of added inorganic phosphate but had no effect in its absence; in the absence of glutamine, glucose did not significantly affect the steady state total adenine nucleotide content. In the absence of Mg²⁺, L-glutamine alone, adenosine alone, or both in combination increased the total adenine nucleotide content, 18, 46, and 58%, resp.; the addition of Mg²⁺ resulted in an additional accumulation of the total adenine nucleotide content, increased the ATP:ADP ratio and the adenine nucleotide quotient but had no effect on glucose utilization or oxygen uptake. Extensive changes in the levels of adenine nucleotide were found in 1 min after addition of 2-deoxyglucose; more than half the ATP content disappeared and ADP and AMP showed a 2- and 3-fold increase, resp., with accompanying decreases in ATP:ADP ratios and adenine nucleotide quotient. The addition of glucose prevented the ATP- and total adenine nucleotide-depleting effects in a 5-min period. Glyoxylate increased AMP and inorganic phosphate levels and had little effect on total adenine nucleotides.

2066 MUCOSUBSTANCES IN NEOPLASM OF THE HUMAN COLON AND RECTUM. (E.) Subbuswamy, S. G. (Newcastle Gen. Hosp., England). *Gut* 12(3):200-207, 1971.

Sections from normal colon and rectum secreted sulfated mucosubstances from the deeper parts of the mucosa and nonsulfated mucosubstances from surface mucosa; little neutral mucosubstance was seen in normal mucosa. Benign colonic and rectal tumors, including adenomatous polyps,

papillary adenomas and villous papillomas, secreted primarily nonsulfated acid mucosubstances, with little sulfated mucosubstances in evidence. When sulfated mucosubstances appeared in association with benign tumors, they were usually confined to deeper parts of the mucosa. Malignant carcinomas of colon and rectum contained very little mucosubstances with 3 of 32 specimens showing almost no secretion. Of the 29 cases of malignancy in which mucosubstances were seen, one case contained only neutral mucosubstance, and 10 were made up of almost entirely acid nonsulfated mucosubstances. No sulfated mucosubstances were seen in 12 cases. In tissue adjacent to tumors, a zone of minimal mucosubstance secretion was seen; outside this zone, most mucosubstances were acid nonsulfated. In other specimens of tissue taken from the vicinity of tumors, mucosubstances were almost entirely sulfated; in the latter areas, secretion of mucosubstances was minimal.

2067 ACTIVITIES OF UREA CYCLE ENZYMES IN TUMOR-BEARING MICE. (E.) Sano, M. (Nagoya U. Sch. Med., Japan). *Nagoya J Med Sci* 33(4):315-28, 1971.

Female SMA mice were given i.p. inoculations of Ehrlich ascites tumor cells to induce tumors and killed 2-16 days after inoculation, at which time arginase activity in their livers was assayed. While arginase activity in livers of tumor-free mice did not vary significantly, arginase activity in Ehrlich tumor-bearing mice increased between 2-16 days postinoculation from a value of 601,000 μ moles of urea formed/100 g body wt/hour at day 2 to 1,338,000 μ moles/100 g/hour at day 16. Tumor-bearing mice showed decreased carcass wt by day 16. In mice with solid tumors which weighed less than 10% of the carcass wt of the mouse, hepatic arginase was comparable to that in tumor-free mice, while in mice bearing solid tumors weighing more than 10% of carcass wt, arginase activity was increased significantly. In a related experiment, mice which had been inoculated with Ehrlich tumor cells were maintained alive and their urine was collected every 2-3 days to determine the rate of urea excretion. Urea excretion in tumor-bearing mice decreased moderately during the period 6-12 days postinoculation, amounting to 96 mg/24 hr/mouse; at 16 day postinoculation, however, urea excretion rose to 147 mg/hr/mouse. Hepatic arginase was markedly increased in tumor-bearing mice on high protein diets and in tumor-free mice given 3 injections of prednisolone hemisuccinate. Arginase activity in the livers of mice given Ehrlich ascites tumor implants and which were adrenalectomized was significantly lower than hepatic arginase activity in tumor-bearing intact mice.

2068 A NEW PROTEOLIPID APPARENTLY ASSOCIATED WITH CANCER. (E.) Skipski, V. P. (Sloan-Kettering Inst. Cancer Res., Rye, N. Y.), M. Barclay, F. M. Archibald, T. P. Lynch, Jr. and C. C. Stock. *Proc Soc Exp Biol Med* 136(4):1261-1264, 1971.

A proteolipid was isolated from lipid extracts of Walker carcinosarcoma by silicic acid column chromatography with stepwise gradient elution in chloroform-methanol mixtures. The lipid was soluble in chloroform-methanol mixtures and insoluble in weak salt or water solutions. The new lipid contained less protein than proteolipids previously isolated from bovine and human nervous tissues. The new lipid was present in transplanted Walker rat tumors and in mouse sarcomas. Of normal tissues, only the spleen had significant amounts of the new lipid. Whole serum lipid extract from tumors contained the new proteolipid. The new lipid was also found in the sera of certain cancer patients; sera from normal subjects was consistently negative for the new lipid.

- 2069 ³⁵SULPHUR UPTAKE IN THE MUCOSA ADJACENT TO CARCINOMA OF THE LARGE INTESTINE. (E.) Filipe, M. I. (Westminster Med. Sch., London, England). *Histochem J* 3(1):27-35, 1971.

Surgical specimens from human carcinoma of the colon and rectum were treated with ³⁵S and the uptake of the isotope was observed in normal mucosa and in mucosa adjacent to the carcinomas. The lower half of the normal colonic crypt contained sulfated acid mucosubstances, and the upper half and surface epithelium of the crypt contained a mixture of sulfated and non-sulfated acid mucins, probably sialic acid residues. In mucosa adjacent to tumors, a gradual decrease of sulfated material was seen together with an increase in a non-sulfated acid mucosubstance which was thought to be sialic acid-rich mucosubstance. ³⁵S was absorbed along the crypt and surface epithelium in normal mucosa; in mucosa adjacent to carcinomas, the isotope was incorporated by surface epithelium only or not at all.

- 2070 REVERSION OF THE INHIBITORY EFFECT OF BUSULPHAN ON BONE MARROW CELL PROLIFERATION BY CHLORAMBUCIL. (E.) Niskanen, E. (2nd Dept. Path., U. Helsinki, Finland), T. Rytömaa and E. Kivilaakso. *Acta Path Microbiol Scand* 79(2): 102-108, 1971.

Male rats were given i.p. injections of 12 mg/kg of busulphan and chlorambucil, and serum drawn from treated rats was incubated with bone marrow cell samples taken at the same time and labeled with ³H-thymidine for monitoring cell proliferation. Serum taken 2-8 days after combined chlorambucil-busulphan treatment did not markedly affect the incorporation of tritiated thymidine into bone marrow cells. By day 8 after treatment, incorporation of label by bone marrow cells incubated with sera from treated rats was 15-97% higher than that in bone marrow cells not incubated with sera from treated rats. Sera taken on day 9 after treatment increased the uptake of ³H-adenine by bone marrow cells by 21.6%. Although before day 9 after treatment, the stimulation of ³H-thymidine by bone marrow cells was more pronounced in cultures incubated with sera taken from rats treated with chlorambucil alone than it was in cultures incubated with sera taken from rats treated with both chlorambucil and busulphan,

by day 9 sera from rats given combined treatment showed the higher values. It was thought that sera from rats given the combined busulphan-chlorambucil treatment contained a proliferation-stimulating factor resembling antichalone.

- 2071 INITIATION OF POLYSOME FORMATION IN MOUSE SARCOMA 180 ASCITES CELLS: UTILIZATION OF CYTOPLASMIC MESSENGER RIBONUCLEIC ACID. (E.) Lee, S. Y. (Tufts U. Sch. Med., Boston, Mass.), V. Krsmanovic and G. Brawerman. *Biochemistry* 10(5): 895-900, 1971.

The study of mRNA-ribosome interaction was studied in mouse sarcoma 180 ascites cells by means of uridine labeling. Incubation of sarcoma cells in the absence of nutrients for 30 min led to nearly complete disappearance of polysomes from the cytoplasm with a return of polysome formation with the addition of nutrients as early as 3 min post-addition with maximum conversion appearing within 10 min. Polysome formation in cells exposed to high levels of actinomycin D followed a similar pattern until a 60-min recovery period had elapsed when monomers again appeared in the treated cells. Heterodisperse RNA-containing structures are apparently released from polysomes during starvation and reutilized for polysome formation after addition of amino acids.

- 2072 THE PRESENCE IN NORMAL LIVER OF HIGHLY ACTIVE CANCER CELL GROWTH INHIBITING SUBSTANCES. (Fr.) Chany, E. (Inst. Cancer Res., Villejuif, France) and C. Frayssinet. *C R Acad Sci* 20:2644-2647, 1971.

The addition of extracts of normal liver cell homogenates from rat, hamster, mouse and beef to cell cultures of rat hepatoma LF, rat, mouse or hamster embryo fibroblasts and KB mouse cells elicited marked inhibition of cell growth. Inhibition was distinctly noticeable at 24 hr and marked at 48 hr. Extracts of hepatoma cells caused no inhibition of the above cells at 24 hr, and only slight effects at 48 hr. The inhibition by liver cell extract of cell growth occurred with 5 µg/ml protein or 50 µg/10⁶ culture cells; hepatoma extracts in amounts of 250 µg/ml protein did not result in marked inhibition of growth. The effects shown were apparently not related to arginase nor to removal of essential cell nutrients by factors other than arginase.

- 2073 HEPATOCELLULAR GLYCOGENOSIS AND HEPATOMA DEVELOPMENT IN MAN. (Ger.) Bannasch, P. (Path. Inst. U. Würzburg, Germany) and O. Klinge. *Virchow Arch Path Anat* 352(2):157-164, 1971.

Electron and light microscopic examinations of biopsy specimens from 12 hepatocellular carcinomas and 5

adenomas in humans were analyzed, with particular reference to glycogen storage. Although the majority were found to be poor in glycogen or glycogen free, 2 carcinomas and 4 adenomas showed massive glycogen storage. The glycogen-poor tumors were composed mainly of basophil cells, with only a few epithelial cells in which glycogen stores could be ascertained. The glycogen-rich cells were found to be close to "clear" cells, and transformation from the light storage cells to the dark tumor cells was frequently observed. In one case it was possible to obtain biopsies at 3 different stages of the tumor development from which it could be seen that the glycogen content varies during the tumor formation. The results confirm the finding in experimental animals that the metamorphosis of the hepatic cells during cancer formation in man is closely related to glycogenesis.

- 2074 POLYAMINE ACCUMULATION AND BIOSYNTHESIS IN A MOUSE L1210 LEUKEMIA. (E.) Russell, D. H. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and C. c. Levy. *Cancer Res* 31(3):248-251, 1971.

Ornithine decarboxylase activity, putrescine synthesis and spermine synthesis were observed in tissues of a rapidly proliferating leukemia induced in mice by the injection of ascites cells 4-10 days prior to the enzyme assay. By 4 days after inoculation with tumor cells, ornithine carboxylase activity in the leukemic mice had attained levels 8 times higher than those attained by normal control mice, but returned to near normal levels by 6 days postinoculation. The enzyme which synthesizes spermidine in leukemic rats was 4-fold above the levels in normal controls by 4 days after inoculation of tumor cells and was still 2-fold above normal at 10 days. The enzyme which forms putrescine was also elevated in leukemic rats. Concentrations of putrescine and spermidine in tumor tissue were increased by nearly 100% over the concentrations of these compounds in any other mouse tissue. Agents which increase the survival time of the tumor-inoculated mice, including 5-[3,3-bis(2-chloroethyl)-1-triazeno]imidazole-4-carboxamide and cytosine arabinoside caused decreases in the ability of the tumor to accumulate polyamines.

- 2075 DIFFUSIBLE FACTORS FROM MALIGNANT CELLS WHICH AFFECT EPIDERMAL SURVIVAL AND DIFFERENTIATION. (E.) Daniel, M. R. (Strangeways Res. Lab., Cambridge, England). *Brit J Cancer* 24(4): 712-718, 1970.

The effect of contact with malignant fibroblasts on embryonic chick epidermis cultured *in vitro* was studied. After 4 days, abnormalities ranging from abnormal differentiation to complete degeneration appeared when epidermal cultures were grown on a 25 μ m-thick cellulose membrane overlying malignant fibroblasts but not on a 50 μ m thick membrane. The use of a semipermeable membrane revealed keratinization without cell degeneration or differentiation. When whole skin was grown on clumps of viable malignant cells, the epidermis remained healthy and may cultures differentiated normally. However,

in some instances epidermal thickening and folding was observed. Malignant dermal fibroblasts apparently produced 2 substances which influenced survival and differentiation of embryonic epidermis; one, of small molecular size, affected the differentiation of the tissue while the other, a macromolecule, caused degeneration.

- 2076 NUCLEIC ACID METABOLISM IN PROLIFERATING AND DIFFERENTIATING COLONIC CELLS OF MAN AND IN NEOPLASTIC LESIONS OF THE COLON. (E.) Troncale, F. (Cornell U. Med. Coll., New York, N.Y.), R. Hertz and M. Lipkin. *Cancer Res* 31(4):463-467, 1971.

Varying levels of thymidine kinase, thymidine phosphorylase and adenine and hypoxanthine phosphoribosyltransferase were found to characterize different stages of cell differentiation in the normal colon. Most cells which synthesized DNA were located in the lower third of the colonic crypts, below cell position 30, while few cells were in DNA synthesis as they reached the upper third of the crypts. In the normal colonic crypt, there was a 4-fold decrease in the activity of thymidine kinase in the upper as compared to the lower third of the crypts, indicating that the level of thymidine kinase activity drops abruptly as cells migrate through the middle third of the crypts. A 4-fold increase in adenine phosphoribosyltransferase was found as cells migrated from the lower to the upper third of the colonic crypts, and a lesser increase was seen in hypoxanthine phosphoribosyltransferase. A decrease in the activity of thymidine phosphorylase was seen as cells migrated to the upper third of the colonic crypts. Comparative enzyme activities were also investigated in cells removed from the surface of the colonic mucosa and from the surface of polypoid lesions having the appearance of adenomas and carcinomas in human subjects. Thymidine kinase activity was greater in villous adenoma and carcinoma cells than in nonneoplastic cells, approximating the levels of activity found in proliferating cells of normal colonic tissue. Adenine phosphoribosyltransferase activity was significantly greater in the mature surface cells of normal colon than in other specimens; activity of this enzyme decreased in cells of polyps of increasing size. Hypoxanthine phosphoribosyltransferase activity was higher in mature colon cells and in small hyperplastic polyps than in the other lesions. The activity of thymidine phosphorylase in hyperplastic tissue was similar to the activity of this enzyme in proliferative cells.

- 2077 THE FORMATION OF MELANIN IN MUSCLE CELLS AFTER THE DIRECT TRANSFER OF RNA FROM HARDING-PASSEY MELANOMA CELLS. (Ger.) Grässmann, A. (Inst. Physiol. Chem., Free U. Berlin, Germany) and M. Grässman. *Hoppe-Seyler Z Physiol Chem* 352(4): 527-532, 1971.

Incubation over 20 hr of cultured Harding-Passey melanoma cells with ^3H -L-DOPA leads to incorporation of isotope (shown autoradiographically) in the cytoplasm of the melanoma cells, but label was not

incorporated over 48 hr incubation by striated muscle cells. The same negative findings were obtained when the isotope was injected by micro-annula directly into the muscle cells. Micro-injection of melanoma cell RNA into the muscle cells prior to incubation with isotope resulted in 80% DOPA incorporation. Alkaline hydrolysis or reaction with ribonuclease of the melanoma cell RNA prior to injection prevented the incorporation of DOPA; pro-nase or DNase treatment had no effect. Injection of rat liver RNA into muscle cells did not elicit isotope incorporation. Cycloheximide prevented incorporation of DOPA into the melanin of Harding-Rassey melanoma cells as well as in muscle cells injected with melanoma cell RNA.

78 PREFERENTIAL INHIBITION BY 5 BROMODEOXY-URIDINE OF THE SYNTHESIS OF TYROSINE AMINO-TRANSFERASE IN HEPATOMA CELL CULTURES. (E.) Stell-gen, R. H. (Dept. Biochem., Biophys., U. California, San Francisco) and G. M. Tomkins. *J Molec Biol* 56(1):177-182, 1971.

rat hepatoma cells incubated for 1 or 2 generations with 5-bromodeoxyuridine (BDU) showed a 75% reduction in tyrosine aminotransferase after 24 hr in culture; replacing BDU with thymidine in the culture medium reversed the BDU effect on tyrosine aminotransferase, and enzyme values returned to normal by 120 hr in culture. Exposure of rat hepatoma cells to BDU for more than 2-3 generations produced a decrease in the rate of cell growth. Total cellular protein and RNA were only slightly reduced in cultures grown with BDU; of 5 other enzymes examined, including 4 dehydrogenases and an acid phosphatase, none showed any change in specific activity for 1-2 cell generations of incubation with BDU. Incorporation of BDU into all DNA seemed to be required in order for it to affect tyrosine aminotransferase. The actual decrease in tyrosine aminotransferase produced by BDU was apparently the result of a lowered rate of synthesis of the enzyme in the cell.

79 THE LYMPHOCYTE AND HUMAN LUNG CANCERS. (E.) Richters, A. (U. Southern California Sch. of Medicine, Los Angeles), R. P. Sherwin and V. Richters. *Cancer Res* 31(3):214-222, 1971.

Lymphocyte interactions were observed among tissue explants taken from human lung epidermoid cancer, adenocarcinoma, undifferentiated carcinoma, and non-neoplastic lung tissues including epithelial cells, spindle cells and macrophages. "Lymphocyte interactions" consisted of random movements of lymphocytes among neoplastic and nonneoplastic human lung cells, and special activities including clustering, congregation and emperipolesis involved attachments of 3 or more lymphocytes to other cells or penetration of lymphocytes into a cell. Lymphocytes were seen to migrate from 82% of cancer tissue explants. Cancer explants showed reduced random and special lymphocyte interactions compared to nonneoplastic tissues; 8% of cancer cells showed random interactions compared

with 15-65% of normal cells, and 17% of cancer cells showed special interactions compared with 10-30% of normal cells. Nonneoplastic cells derived from cancer-free subjects showed more random lymphocyte interactions than nonneoplastic cells derived from cancer-bearing subjects; this relationship between cancer-free and cancer-bearing subjects' nonneoplastic cell explants was reversed for special lymphocyte interactions. Nonneoplastic cells from cancer-bearing subjects with adenocarcinoma or undifferentiated carcinoma had random lymphocyte interaction levels of 34.8 and 13.8%, resp., while random interaction levels for nonneoplastic cells from patients with epidermoid cancer were less than 1%. Random lymphocyte interactions for epidermoid cancer cells were 3 times higher than for adenocarcinoma cells, and 5 times higher than for undifferentiated cancer cells; special lymphocyte interactions were lower in epidermoid cancer cells than in the other 2 types of cancer cell. Among the special lymphocyte interactions, emperipolesis was the dominant response to cancer cells.

2080 A HISTOCHEMICAL STUDY OF ALKALINE AND ACID NUCLEASE ACTIVITY IN THE HUMAN BRAIN COMPARED TO THE INCIDENCE OF MALIGNANT TUMOURS. (E.) Taper, H. S. (Dept. Neuropath., U. Louvain, Belgium), J. M. Brucher and G. Doyen. *J Neurol Sci* 12(4):369-382, 1971.

Acid and alkaline nuclease activity was assayed in various parts of the normal brain, and associations of acid and alkaline nuclease with brain tumors were explored. The greatest alkaline DNase activity was found in the epithelial cells of the choroid plexus; the apical region of the ependymal epithelium was found to have high alkaline DNase in the cytoplasm of cells, but not in cell nuclei. Brain capillaries, neurons and glial cells were practically negative for alkaline DNase, while leptomeninges showed alkaline DNase activity. Alkaline RNase was distributed in the brain in a manner similar to the distribution of alkaline DNase; however, RNase was present in the endothelial cells of brain capillaries, but alkaline DNase was not. Acid DNase was present in all nerve cells; glial cells had lower levels of acid DNase than nerve cells. Acid RNase was distributed in a manner similar to the distribution of acid DNase. It was found that glial cells, which displayed a low nuclease activity, had a high incidence of malignant tumors, accounting for 26.5% of one series of malignancies. Nerve cells, on the other hand, which demonstrated the highest values for nuclease activity, had the lowest incidence of malignant tumors of all the brain tissues (0.0%).

2081 INCORPORATION OF ^{32}P INTO NUCLEIC ACIDS IN MAMMARY TISSUE OF MICE SUSCEPTIBLE AND RESISTANT TO BREAST CANCER. (E.) Sheth, N. A. (Cancer Res. Inst., Tata Mem. Ctr., Bombay, India), S. V. Bhide and K. J. Ranadive. *J Nat Cancer Inst* 46(4):731-734, 1971.

Mammary tumor-susceptible C3H strain mice, and mammary tumor-resistant C57B1 mice, were given i.p.

injections of 15 μC ^{32}P -labeled sodium phosphate solution; intact and castrate mice 4, 8 and 12-month-old were used. The incorporation of ^{32}P into DNA and RNA of mammary and tumor tissue were compared in the susceptible and resistant strains. In tumor-bearing C3H mice, DNA and RNA in tumor tissue incorporated more label than did other tissues. In both strains, the uptake of ^{32}P into DNA was similar in 4- and 8-month-old mice, and in corresponding C3H groups. In castrate C57Bl mice, the uptake of ^{32}P into DNA in 8-month-old mice was markedly lower than in 8-month-old intact mice, and continued to be low in 12-month-old castrates. Incorporation of ^{32}P into RNA in 8-month-old castrates was comparable to that in 8-month-old intact mice, but incorporation into RNA fell significantly in 12-month-old C57Bl castrates.

- 2082 DEOXYRIBONUCLEIC ACID POLYMERASE ACTIVITY ASSOCIATED WITH A PLASMA PARTICULATE FRACTION FROM PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA. (E.) Kiessling, A. A. (Dept. Agric. Chem., Oregon St. U., Corvallis), G. H. Weber, A. O. Deeney, E. A. Possehl and G. S. Beaudreau. *J Virol* 7(2):226, 1971.

DNA polymerase activity in human plasma from patients with chronic lymphocytic leukemia was studied by buoyant density determination and enzyme assay. Enzyme activity from the plasma of an 87-yr-old male diagnosed as having had chronic lymphocytic leukemia for 10 yr without chemotherapy was found to be (by ^3H -dGTP incorporation) 72-125 cpm without detergent, compared to 47-570 cpm with detergent treatment. The polymerase activity of the plasma from a newly diagnosed patient under transfusion therapy during the plasma collection period showed label incorporation ranging from 50-84 cpm without detergent and 80-170 cpm with detergent treatment; in both instances enzyme activity was stimulated by the addition of *Micrococcus lysodeikticus* DNA to the assay mixture, which resulted in increases from 76-525 cpm in the first case and 48-135 cpm in the second case. Banding on isopycnic cesium chloride showed a major band at a density of 1.72 with considerable radioactivity located in the dense regions of the gradient with DNA from one case, and enzyme from this individual had a high rate of DNA synthesis. Absence of particulate enzyme activity in plasma from healthy individuals demonstrated that the activity from the leukemic plasmas was not a measure of low enzyme activity normally found in plasma. However, the possibility that the appearance of DNA polymerase in the plasma particulate fraction from the patient with a 10-yr history of chronic lymphocytic leukemia may have been a secondary effect from the stress of the disease.

- 2083 IMP: AND AMP:PYROPHOSPHATE PHOSPHORIBOSYLTRANSFERASE IN LEUKEMIC AND NORMAL HUMAN LEUKOCYTES. (E.) Smith, J. L. (U. Cambridge Dept. Med., England), G. A. Omura, I. H. Krakoff and M. E. Ballis. *Proc Soc Exp Biol Med* 136(4):1299-1303, 1971.

Leukocytes isolated from venous heparinized blood were incubated with adenine-8- ^{14}C and hypoxanthine-8- ^{14}C and nucleotide formation was determined. The incorporation of substrate at concentrations of 100 μM in the medium was linear over the range 0-6 x 10⁶ leukocytes/ml. The mean peripheral blood leukocyte hypoxanthine-guanine phosphoribosyltransferase activity of 9 patients with acute myelogenous leukemia in bone marrow relapse was significantly greater than normal (0.01 > p > 0.001); the mean activity in leukocytes from patients with acute lymphoblastic leukemia in marrow relapse was somewhat higher than normal level. Leukocytes from all patients had increased mean level of adenine transferase; however, the activities were not significantly greater than normal. The activity of adenine phosphoribosyltransferase was 2.8-7.2 times as great as hypoxanthine phosphoribosyltransferase in normal leukocytes; patients with leukemia showed an adenine enzyme activity of 0.7-7.5 times as active as the hypoxanthine enzyme. Activities did not appear to be correlated to drug therapy or the peripheral cell counts of the patients studied.

- 2084 STUDIES ON β -GLUCURONIDASE AND DNA SYNTHESIS ACTIVITIES IN THE BLADDER TUMORS. (E.) Senda, H. (Sch. Med. Nagoya U., Japan). *Nagoya J Med Sci* 33(3):203-229, 1971.

Twenty-four hour urine specimens from patients, blood serum, exudate from temporary excluded bladders and biopsy material from a bladder carcinoma were studied for β -glucuronidase activity by means of the aglucuron method, disc electrophoresis and autoradiography. β -Glucuronidase activity tended to be high in the morning and low in the afternoon as determined at 3-hr intervals for 24 hr. Enzyme activity in the serum was not always high when activity was high in the urine; no definite pattern of fluctuation was seen. The unit volume activity of the enzyme in 5 patients showed greater day-to-day fluctuation than did the urine enzyme activity. The presence of bacteria in 2 cases revealed increased urinary activity in proportion to the incubation time even though bacterial cultures at the end of 24 hr were negative. Right and left renal urine obtained by ureteral catheter in 5 persons without disease showed no difference in activity from bladder urine, whereas in the presence of bladder tumors β -glucuronidase activity of bladder urine was remarkably high compared to ureteral urine. In normal subjects the minimum value for urinary glucuronidase was 0.10 $\mu\text{g}/\text{ml}/\text{hr}$ and the maximum value was 1.45 $\mu\text{g}/\text{ml}/\text{hr}$ in comparison to serum activity which ranged from 0.18 to 0.84 $\mu\text{g}/\text{ml}/\text{hr}$. In 38 cases of bladder tumor urinary enzyme activity ranged from 1.01 $\mu\text{g}/\text{ml}/\text{hr}$ to 13.40 $\mu\text{g}/\text{ml}/\text{hr}$; administration of D-glucaro-dilactone suppressed these values to normal levels.

- 2085 β -GLUCURONIDASE ACTIVITY IN TUMORS: ACCUMULATION OF RADIOIODINATED PHENOLPHTHALEIN. (E.) Anghileri, L. J. (U. Colorado Med. Ctr., Denver) and E. S. Miller. *Oncology* 25(1):19-32, 1971.

the use of ^{131}I -phenolphthalein glucuronide as a labeling substrate in tumor detection on the basis of β -glucuronidase activity has been studied in Ehrlich carcinoma and melanoma B16-bearing mice following i.p. and i.v. injection. *In vivo* radioactivity distribution 24 hr after i.v. injection decreased as follows: kidney>liver>spleen>tumor>lungs>intestine>pancreas>blood>muscle>stomach; "free" iodide assay produced by the *in vitro* action of β -glucuronidase on labeled glucuronide indicated that only stomach tissue showed deiodinating activity. The stability of the radioiodine tag was also reflected in the whole body counting, in which up to 23% of the activity remained at 30 days after injection; 2 to 7% of the counts was deposited in the liver. Higher radioactivity accumulation in liver, kidneys and intestine was due mainly to their function as detoxication and/or elimination organs; generally, the localization of ^{131}I -phenolphthalein glucuronide in tumors appears to be an excellent index of its β -glucuronidase activity.

2086 GLYCOGEN SYNTHESIS AND GLYCOGEN SYNTHETASE IN RAT ASCITES HEPATOMAS OF LOW AND HIGH GLYCOGEN CONTENT. (E.) Saheki, R. (Res. Inst. Tuberc. Leprosy, Cancer, Tohoku U., Sendai, Japan), Sato and S. Tsuiki. *Biochim Biophys Acta* 230(3): 571-582, 1971.

Male Donryu rats maintained on a commercial rat diet and given glycogen-rich and glycogen-deficient tumor inoculation were used as hosts for tumor cells which were harvested from the peritoneal cavity 4-6 days after inoculation and incubated *in vitro* in either the presence or absence of labeled glucose. In the presence of glucose, glycogen synthesis was initiated at comparable rates in both cell lines, but in the glycogen-deficient line the synthesis rate declined at comparable rates in both cell lines; and in the glycogen-rich tumor the rate of synthesis remained unaffected by glycogen accumulation. In the presence of amygdalin the glycogen-rich tumor cells remained unaffected while those of the glycogen-deficient tumor failed to synthesize glycogen from glucose. The glycogen-rich cells had higher levels of glycogen synthetase activity and lower levels of phosphorylase activity than the glycogen-deficient hepatoma, while the phosphoglucosyltransferase activities in the 2 hepatomas were similar. The glycogen synthesis in the glycogen-rich cells appears to be somewhat insensitive to cellular glycogen level, suggesting the absence or deficiency of such a feedback mechanism.

2087 TRANSFER AND RIBOSOMAL RIBONUCLEIC ACIDS IN BRAIN TUMORS. (E.) Viale, G. L. (Neurosurg. Clin., U. Genoa, Italy), H. Kroh, G. Grosso and E. Viale. *Neurosurg* 34(3): 446-447, 1971.

Methylation of transfer and ribosomal ribonucleic acids and methylase activity in human gliomas has been studied by means of infrared spectrophotometry. Transfer RNA of malignant gliomas presented a higher content of methylated nucleosides proportional to

the degree of malignancy and varied with the type of tumor, whereas ribosomal RNA did not show striking differences. The increased content of methylated nucleosides appeared to indicate increased non-tissue-specific tRNA methylase activity in all types of tumors.

2088 ASSAY OF tRNA METHYLASE ENZYMES IN STUDIES OF MALIGNANT TRANSFORMATION *IN VITRO*. (E.) Pillinger, D. J. (Christie Hosp., Manchester, England) and R. Wilkinson. *Life Sci* 10(5):241-249, 1971.

A normal clone of hamster kidney cells, a spontaneously transformed line of cells, and a line of cells derived from a cheek pouch tumor were cultured and treated with S-adenosyl-L-methionine (methyl- ^{14}C); the uptake of that agent by methyl deficient *E. coli* transfer RNA (tRNA) was used to measure the tRNA methylase activity in normal and neoplastic hamster cells. Supernatant fractions from the neoplastic cells incorporated twice as much of the labeled methyl group into the methyl deficient *E. coli* tRNA as did supernatants from normal cells. Cheek pouch tumor cells were more active than spontaneously transformed cells. tRNA methylase activity was found to be higher in kidney tissue from newborn hamsters than in kidney tissue from adults.

2089 SEROLOGIC SPECIFICITIES OF METHYLATED BASE IMMUNE SYSTEMS. (E.) Levine, L. (Grad. Dept. Biochem., Brandeis U., Waltham, Mass.), H. Van Vunakis and R. C. Gallo. *Biochemistry* 10(11):2009-2013, 1971.

New Zealand albino rabbits were immunized with 1.0 ml of complete Freund's adjuvant containing 5 mg of 1-methylguanosine, N²-methylguanosine, N²-dimethylguanosine, 7-methylguanosine or 5-methylcytidine injected once into the toepads and once i.m. each wk for 3 successive wks; the rabbits were bled from the ear 1, 2 and 3 wk subsequent to the final injection. The antibodies were directed toward the methyl group on the C-1 position of each of the methylated nucleoside-human serum albumin. Whereas the methylated guanosine immune systems were relatively easy to inhibit with the homologous nucleoside (50% inhibition ranging from 30-50 nmoles), this methylated cytosine immune system was more difficult to inhibit with its homologous nucleoside (2000 nmoles required for 50% inhibition). If the tRNAs of neoplastic tissue contain methylated bases which differ from normal tissues, the amount of these bases and the ratio of one base to another in biological fluids may be indicative of the presence and/or relative amounts of the abnormal growth.

2090 ALTERATIONS IN SPECIFIC TRANSFER RIBONUCLEIC ACIDS IN A SPECTRUM OF HEPATOMAS. (E.) Srinivasan, D. (Coll. Phys. Surg. Columbia U., New York, N.Y.), P. R. Srinivasan, D. Grunberger, I. B. Weinstein and H. P. Morris. *Biochemistry* 10(11):1966-1973, 1971.

The tRNAs for tyrosine, histidine, asparagine, and phenylalanine of five Morris hepatomas grown i.m. in the thigh muscle of male rats of the inbred ACI T² strain and the Buffalo strain were compared to the corresponding tRNAs from livers of normal rats of the same strains, sex and age. Tyrosyl-tRNA from hepatoma 3924A eluted at a higher salt concentration than that from the control rat liver; no difference was seen in hepatomas 9121, 3683F and 5123C from control profiles. Tyrosyl-, histidyl- and asparaginyl-tRNA eluted at a higher salt concentration from hepatoma 3924A, whereas the phenylalanyl-tRNA profile was identical with that of normal liver. The other hepatomas showed only altered phenylalanyl-tRNA profiles, which eluted earlier than the controls. The codon recognition properties of tyrosyl-tRNAs from Novikoff hepatoma, hepatomas 3924A and 9098, and normal rat liver were also examined. The normal tyrosine codons UAU and UAC were recognized by all of the tyrosyl-tRNAs with the greater response being shown to UAU and with no response to the chain terminator codons UAG and UAA. These results indicate that these tRNAs are not the same as the tyrosyl-tRNA nonsense suppressors of bacteria.

- 2091 THE TRANSFER RNA METHYLASES OF HUMAN LYMPHOCYTES: II. DELAYED INDUCTION BY PHA IN LYMPHOCYTES FROM PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA. (E.) Riddick, D. H. (U. Virginia Med. Sch., Charlottesville) and R. C. Gallo. *Blood* 37(3):293-298, 1971.

When peripheral blood from patients with untreated chronic lymphocytic leukemia (CLL) was centrifuged and the lymphocytes were treated with phytohemagglutinin (PHA), the specific rate of transfer RNA (tRNA) methylases in lymphocytes treated with PHA for 120 hr was 5 times the rate of tRNA methylase in CLL lymphocytes not treated with PHA. In addition, the extent of tRNA methylation was 400% higher in PHA-stimulated CLL lymphocytes than in controls. Cells incubated in cultures without PHA were small mature lymphocytes, while PHA-stimulated cells showed 8.2% large transformed cells. Blastic transformation of CLL lymphocytes cultured with PHA proceeded at a slower pace than PHA-stimulated lymphocytes of normal subjects; CLL lymphocytes attained maximal transformation rates after 168 hr in culture with PHA, while PHA-treated lymphocytes of normal subjects reached maximal transformation rates after 40 hr in culture. Levels of tRNA methylase were similar in normal and CLL lymphocytes without PHA stimulation. The increase in the activity of tRNA methylase in PHA-stimulated CLL lymphocytes may be associated with enzymes which were not present prior to PHA treatment, suggesting that PHA induces quantitative and qualitative changes in tRNA methylase enzymes of CLL lymphocytes.

- 2092 CHROMOSOMAL ABERRATIONS AND THEIR RELATION TO MALIGNANCY IN MENINGOMAS: A MENINGIOMA WITH RING CHROMOSOMES. (E.) Mark, J. (Inst. Path., U. Lund, Sweden). *Acta Path Microbiol Scand* 79(2): 193-200, 1971.

Karyotype studies were carried out on cells from a benign human syncytical meningioma; tumor cells maintained *in vitro* were examined in 3 fixations made 5, 37 and 88 days after explanation of the tumor. In the first fixation, nearly 50% of the cells had the stemline number 42 with a minor second mode at stemline number 45. The stemline karyotype in this fixation contained a large ring chromosome; the ring was also seen in triploid and hypotetraploid cells in the first fixation. Seventy-five percent of cells, the stemline, possessed the ring chromosome while 25% of cells, the sideline population, lacked it. In the second fixation, the hypodiploid stemline found in fixation 1 had disappeared and was replaced by a 46-chromosome stemline; however, the hypodiploid sideline with chromosome number 45 persisted. The 45-chromosome sideline lacked a G chromosome in all 3 fixations. It was thought that the persistence of the sideline may have been a result of the persistence of a remnant of a stemline developed in the *in vivo* growth of the meningioma. Outgrowth of stroma cells may have been responsible for the shift in stemline characters.

- 2093 GENETIC PREDISPOSITION TO MELANOMA AND OTHER SKIN CANCERS IN AUSTRALIANS. (E.) Lane Brown, M. M. (Massachusetts Gen. Hosp., Boston), C. A. B. Sharpe, D. S. Macmillan and V. J. McGovern. *Med J Aust* 58(16):852-853, 1971.

A survey of 1,433 patients from the Sydney, Australia area with melanomatous cutaneous metastases, non-cutaneous cancer, basal cell carcinoma or squamous cell carcinoma was conducted to determine the prevalence of melanoma among Australians of Celtic ancestry. Celtic ancestry was ascertained by noting the surnames of patients in the survey. Persons of Celtic genetic heritage were disproportionately represented among patients with skin cancer, including melanoma. Fifty percent of the patients with melanomatous cutaneous metastases were of Celtic descent, as were 43% of the patients who had died from melanoma. Forty-eight percent of the patients with basal cell carcinoma were Celtic, and 47% of the patients with squamous cell carcinoma were Celtic. The percentages of persons with a Celtic background among those with skin cancer, including melanoma, was almost twice the figure obtained for persons of non-Celtic heritage.

- 2094 SOME PRELIMINARY OBSERVATIONS ON THE INFLUENCE OF GENETIC ADMIXTURE ON CANCER INCIDENCE IN AMERICAN NEGROES. (E.) Petrakis, N. L. (U. California Sch. Med., San Francisco). *Int J Cancer* 7(2):256-258, 1971.

A correlation was found between degree of admixture of white with American Negro genes and incidence of breast cancer. Genetic admixture was measured by observing the frequency of the Duffy Fy(a⁺) gene, which is present in white populations and absent in African Negroes (the frequency of the Duffy gene in the United States whites was taken as unity). Afri-

an Negroes with zero genetic admixture showed 9 cases of breast cancer/100,000 population; American Negroes with genetic admixtures of 0.106, 0.219 and 0.260 had breast cancer incidences of 38.5, 43.3 and 44.6 cases/100,000 population, resp. Whites had an incidence rate for breast cancer of 69 cases/100,000 population. No correlation was found between genetic admixture and cervical cancer, rectal cancer, lung cancer, stomach cancer, esophageal cancer or prostatic cancer.

95 A SPECIFIC COMMON CHROMOSOMAL PATHWAY FOR THE ORIGIN OF HUMAN MALIGNANCY: II. (E.) Minkler, J. L. (Lawrence Radiat. Lab., California, Livermore), J. W. Gofman and K. Tandy. *Brit J Cancer* 24(4):726-740, 1970.

The relationship of excess E16 chromosome and human cancer was studied in fresh cancer tissue obtained from surgical specimens on the basis of chromosome length and centromeric index. All cell lines studied only the E16 chromosome class showed a mean chromosome number per cell elevation with a mean E16 level 2.03 times the "corrected E16 expectation" *in vitro*; in 10 of 11 fresh cancers absolute E16 chromosome levels were significantly elevated, and "corrected expectation" figures showed significant E16 chromosome elevation.

96 HUMAN LEUKEMIA: GENETIC AND ENVIRONMENTAL CLUSTERS. (E.) Heath, C. W., Jr. (Natl. Communicable Dis. Ctr., Atlanta, Ga.). *Bibl Haemat* 649-653, 1970.

An instance of leukemia or lymphoma occurring in members of a sibship and an instance of lymphosarcoma arising in 4 persons associated with a herd of lymphosarcoma-affected dairy cattle are reported. In the sibship, 5 of 12 sibs had died of leukemia or lymphoma; there were 2 cases of chronic lymphocytic leukemia, 1 case of lymphocytic lymphoma, and 2 cases of reticulum cell sarcoma. Of the 4 surviving cows, all had low IgG immunoglobulin levels and decreased delayed hypersensitivity responses; 2 sibs had decreased lymphocyte transformation and increased lymphocytes in the bone marrow. The results suggest that the surviving sibs are in a pre-leukemic state. Four cases of lymphosarcoma occurring in a population of 200 living in the vicinity of a lymphosarcoma-affected dairy herd represented a significant increase over the expected lymphosarcoma incidence. The dairy herd in question consisted of 250 cows in which 1 case of lymphosarcoma had occurred per yr.

97 ENZYMIC MODIFICATION OF CHROMOSOMAL MACROMOLECULES: II. THE FORMATION OF HISTONE 3-METHYL-L-LYSINE BY A SOLUBLE CHROMATIN METHYLASE. (E.) Burdon, R. H. (Dept. Biochem., U. Glasgow, Scotland) and E. V. Garven. *Biochim Biophys Acta* 232(2):371-378, 1971.

Chromatin preparations from Krebs 2 ascites cells devoid of histone were incubated with methyl-labeled S-adenosyl-L-methionine and assayed for their ability to catalyze the transfer of methyl groups of protein; the resulting amino acids were analyzed by paper electrophoretic and chromatographic techniques to determine the nature of the product. Initially methyl uptake was low and then showed a dramatic increase with the addition of calf thymus histone at an optimal pH8. Methylation was reduced 96% when the reaction mixture was heat-treated at 100% for 5 min. Cytochrome c, ribonuclease, trypsin inhibitor, bovine serum albumin, lysozyme, γ -globulin, apoferritin, β -galactosidase, poly L-arginine or poly L-lysine had no effect on uptake and increasing concentrations of Mg^{+2} were somewhat inhibitory. No inhibition was noted in the presence of sodium formate, aminopterin or pyromycin. Only $1/3$ of the labeled product was associated with histone; the rest of the label appeared in an acid-insoluble protein as ϵ -N-trimethyl-L-lysine.

2098 LONG ACROCENTRIC MARKER CHROMOSOMES IN MALIGNANT EFFUSIONS AND SOLID TUMORS. (E.) Benedict, W. F. (Natl. Inst. Hlth, Bethesda, Md.), C. D. Brown and I. H. Porter. *New York J Med* 71(9):952-955, 1971.

Karyotype analysis of cells in effusions from 24 malignant tissue specimens, including breast carcinomas, cervical carcinoma and lung carcinoma, showed a long acrocentric marker chromosome in 75% of metaphases. Eleven of 18 solid tumors (61%), including osteogenic sarcoma, bronchogenic carcinoma, malignant lymphoma and transitional-cell carcinoma were found to have long acrocentric marker chromosomes (direct and short-term cultures).

2099 A HUMAN TISSUE CULTURE CELL LINE FROM A TRANSITIONAL CELL TUMOR OF THE URINARY BLADDER: GROWTH, CHROMOSOME PATTERN AND ULTRASTRUCTURE. (E.) Rigby, C. C. (St. Paul's Hosp., London, England) and L. M. Franks. *Brit J Cancer* 24(4):746-754, 1970.

The cytological behavior of urothelial neoplasms *in vitro* and *in vivo* was studied in cell cultures from 18 human bladder tumors. Three cell lines were maintained for 7 transfer generations; each had a fibroblastic morphology and a normal diploid karyotype, and a 4th line was maintained in continuous culture. In the primary and first subcultures the cells had a predominantly epithelial pattern with patches of fibroblast-like cells which disappeared in succeeding cultures. Nucleoli were large and usually single with foamy cytoplasm containing glycogen granules and few fat droplets. Cells from the 6th and 7th transfer generations used for heterotransplantation developed tumor nodules resembling the primary tumor in 3 of 15 hamsters inoculated after 21, 40 and 259 days resp. Chromosome analysis in the early stages of culture showed the presence of the stemline number and karyotype as was demonstrated in later transfer generations with a mode of 48 and 60% adherence to

a pattern in which there was an extra chromosome in Group C and in Group D, and only occasionally marker chromosomes.

- 2100 ENZYMIC MODIFICATION OF CHROMOSOMAL MACROMOLECULES: I. DNA AND PROTEIN METHYLATION IN MOUSE TUMOUR CELL CHROMATIN. (E.) Burdon, R. H. (Dept. Biochem., U. Glasgow, Scotland). *Biochim Biophys Acta* 232(2):358-370, 1971.

Chromatin preparations from Krebs 2 ascites cells were incubated with ^3H -methyl-labeled S-adenosyl-L-methionine at 37°, 23° C and at room temperature for varying times in preparation for chromatographic and electrophoretic analysis. Maximum level of label incorporation was obtained at 10-20 min at 37°; 40% of these methyl groups were rendered acid-soluble in hot 15% trichloroacetic acid. The addition of pancreatic deoxyribonuclease increased the label uptake into alkali-stable, acid precipitable material, while ribonuclease had no effect; snake venom diesterase augmented label incorporation and could be correlated with the loss of DNA from the chromatin fraction. Deoxyribonuclease produced maximal stimulation and caused all radioactivity to be alkali-stable and precipitable when heated at 100° for 5 min following treatment with 15% trichloroacetic acid. The bulk of the ^3H radioactivity chromatographed with a fraction almost corresponding to lysine. Examination of the hydrolysis products of the protein fraction incubated for 2 hr at 37° without deoxyribonuclease revealed ^3H radioactivity in regions corresponding to ϵ -N-methyl-L-lysine in addition to the ϵ -dimethyl- and ϵ -trimethyl- regions. Addition of homologous DNA increased the level of DNA methylation, whereas calf thymus DNA was less effective; no stimulatory effect was noted with the addition of bacterial DNA, which produced inhibitory effects in some cases. Methylation of DNA and protein showed an inverse proportion at 37°; at 23°, although the total label incorporation was not significantly different, the proportion incorporated into the protein was greater.

- 2101 A SPECIFIC COMMON CHROMOSOMAL PATHWAY FOR THE ORIGIN OF HUMAN MALIGNANCY: II. EVALUATION OF LONG-TERM HUMAN HAZARDS OF POTENTIAL ENVIRONMENTAL CARCINOGENS. (E.) Minkler, J. L. (Lawrence Radiat. Lab., U. California, Livermore), J. W. Gofman and R. K. Tandy. *Advances Biol Med Phys* 13:108-151, 1970.

Fresh cancer tissue from 11 patients with positively diagnosed malignant effusions or solid cancers, bone marrow from an untreated case of chronic granulocytic leukemia, and a suspension culture from Burkitt's lymphoma were studied for chromosome length and centromeric index. The only chromosome showing significant elevation or depression in all cell lines studied was E16; the elevation in mean number of chromosomes/cell was highly significant in every case, and averaged 3.10-fold for the entire group. All but one cell line showed a mean total number of chromosomes greater than the 46 chromosomes characteristic of normal cells,

and the E16 elevation was significantly and appreciably greater than that expected from the elevation in the total number/cell. Similar results were obtained in chromosome preparations made 2-20 hr after excision of fresh cancer tissue or withdrawal of the malignant effusion in 10 of the 11 biopsies studied; the 11th specimen revealed a value of 37.13 total chromosomes/cell; however, the E16 level, when compared to the total number, was significantly high. No other chromosome class showed consistent elevation or depression. Chronic granulocytic leukemia cells failed to show elevated numbers of E16 chromosomes. Chromosome numbers in cells from Burkitt's lymphoma were normal, and each cell showed a specific marker chromosome, the content of which is unknown.

- 2102 LIPOGRANULOMAS IN HUMAN LIVER BIOPSIES WITH FATTY CHANGE: A MORPHOLOGICAL, BIOCHEMICAL AND CLINICAL INVESTIGATION. (E.) Christoffersen, P. (Commun. Hosp. Copenhagen, Denmark), O. Braendstrup, E. Juhl and H. Poulsen. *Acta Path Microbiol Scand* 79(2):150-158, 1971.

Of 67 percutaneous human liver biopsies showing fatty change, 43 contained lipogranulomas presenting one of 3 typical features: some lipogranulomas consisted of a single nodule with a large extracellular vacuole surrounded by histiocytes, some consisted of a solitary nodule composed of histiocytes of which the majority were lipophages or lymphocytes, and others were multinodular structures composed of confluent nodules of both or either of the first 2 types. Lipogranulomas of the second type were thought to have developed from lipogranulomas of the first type. Ninety-eight percent of liver biopsies with lipogranulomas and 54% of those without lipogranulomas showed lytic necroses; 28% of lipogranulomatous biopsies contained acidophilic bodies, while none of the lipogranuloma-free biopsies contained acidophilic bodies. Kupffer cell proliferation was seen in all lipogranulomatous biopsies and by 21% of lipogranuloma-free biopsies. There was no significant difference between the 2 groups of biopsies regarding the incidence of portal fibrosis, bile duct proliferation, cholestasis, siderosis and content of lipofuscin. Biochemical tests showed that serum aspartate transaminase was higher in the group of biopsies with lipogranulomas than in the group of biopsies without lipogranulomas. Multinodular lipogranulomas were thought to be more likely to develop connective tissue in the liver parenchyma than single-nodular lipogranulomas, which often disappeared without serious complications.

- 2103 FINE STRUCTURE OF AN OAT CELL CARCINOMA OF THE LUNG ASSOCIATED WITH ECTOPIC ACTH SYNDROME. (E.) Corrin, B. (St. Thomas Hosp. Med. Sch., London, England) and M. McMillan. *Brit J Cancer* 24(4): 755-758, 1970.

Human pulmonary oat-cell carcinoma associated with ectopic adrenocorticotrophic hormone syndrome was studied electron-microscopically. The fine structure showed abundant free ribosomes and lack of inter-

cellular connections, with small dense cytoplasmic granules, identical to those of non-secretory oat-cell carcinomas. In this hormonally active tumor, the granules were more numerous, suggesting a secretory nature. The tumor produced a negative silver reaction. Common histogenesis for cells with this type of secretory granule cannot be claimed in view of their presence in mesothelioma.

04 ELECTRON MICROSCOPY OF GLYCOGEN IN MENINGO-
 GOTHelial MENINGIOMA. (E.) Koizumi, J.
 Arch. Med. Chiba U., Japan) and S. Minei. *Arch*
Stol Jap 32(4):347-354, 1970.

Three human meningotheial meningiomas were excised and prepared for electron microscopy; the tumor cells were found to contain glycogen in varying amounts. Glycogen was found in cytoplasmic granules which showed an affinity for lead staining. In some cases, glycogen granules occupied practically the entire cytoplasmic matrix; in other cases, glycogen granules were diffused throughout the cytoplasm and the processes, while in other cells no glycogen granules could be seen. Glycogen granules were both single and compound. Cell metabolism of a neoplastic character may have produced abnormal carbohydrate metabolism in certain of the cells, leading to the observed variation in the distribution of glycogen granules.

05 CARCINOMA OF THE PANCREAS, INFANTILE TYPE:
 A LIGHT AND ELECTRON MICROSCOPIC STUDY.
 Fable, W. J. (Med. Coll. Virginia, Richmond),
 J. S. Still and S. Kay. *Cancer* 27(3):667-673,
 1971.

Sections from an islet cell adenoma of the pancreas arising in a 4-yr-old girl were examined by electron microscopy; it was found that the tumor invaded the superior mesenteric vein and the wall of the transverse colon. Two patterns of cell growth were found in the tumor material: small cells growing in an acinar and cord-like pattern, and spindle and squamoid cells. Glycogen was found in the tumor cells. Ultrastructurally, the tumor was seen to contain uniform cells surrounding small lumina; the luminal surface of the cells had microvilli. The microscopic picture suggested that the tumor at hand originated in the duct cells and showed some differentiation in the direction of acinar cells.

06 ELECTRON MICROSCOPIC STUDY OF BASAL CELL
 CARCINOMA. (E.) Ishibashi, A. (Nihon U.
 Med., Tokyo, Japan), T. Kasuga and E. Tsuchiya.
Invest Derm 56(4):298-304, 1971.

Electron microscope inspection of samples from 3 basal cell carcinomas showed stromas consisting of granular and amorphous materials including glomerular masses; this material was seen in widened intercellular spaces as well as in stroma, and was thought to represent mucopolysaccharides revealed by metachromasia. Transparent bodies composed of

a glassy amorphous matter or of multiple tubular membranous structures were seen in the surfaces of plasma membranes; it was speculated that this amorphous material was related to metachromasia, perhaps reflecting secreting activity of the neoplastic cells. The cytoplasmic matrices of the tumors were found to contain cytolytic caverns filled with material of low electron density. Melanin granules undergoing digestion were seen in the neoplastic keratinocytes; premelanosome-like granules were also seen.

2107 ELECTRON MICROSCOPIC STUDIES OF THE TRANSMISSIBLE SARCOMA IN DOGS. (Rus.) Shubin, A. S. (Inst. Exp. and Clin. Oncol. Acad. Med. Sci. Moscow, U.S.S.R.) and V. I. Ponomar'kov. *Arkhl Patol* 33(3):38-42, 1971.

The morphology and ultrastructure of transmissible sarcoma (Sticker's tumor) was investigated in 5 dogs. The tumors consisted of large flattened cells with a light cytoplasm and a round nucleus. Papillary structures were noticed near the cell surface and an alveolar constitution within the deeper layers of the tumor was observed. Electron microscopy revealed small vacuoles within the cytoplasm; both vacuoles and cytoplasm exhibited fine fibrillar structures. The Golgi apparatus appeared to be scarce and was represented by a hypertrophic vesicular component. Unusual parallel rows of membrane complex-like formations were also noticed within the cytoplasm. The widening of some of these membranes led to the formation of vacuoles. The nature and possible relationship of these membranes to the Golgi apparatus or to the endoplasmic reticulum is discussed.

2108 THE TWO VARIETIES OF LYMPHOID TISSUE
 "RETICULOSARCOMAS", HISTIOCYTIC AND
 HISTIOBLASTIC TYPES. (E.) Mathe, G. (Hosp. Paul
 Brousse, Villejuif, France), R. Gerard-Marchant,
 J. L. Texier, J. R. Schlumberger, L. Berumen and
 M. Paintrand. *Brit J Cancer* 24(4):687-695, 1970.

Histological and cytological examinations were performed on 110 sections and smears of reticulosarcomas; this nosological entity was subdivided into 2 classes, histiocytic and histioblastic reticulosarcoma, on the basis of the examination. Histiocytic sarcomas often presented an intense network of reticulin with 60% of histiocytic sarcomas and only 4% of histioblastic sarcomas containing reticulin. Histioblastosarcoma was found to be more frequent than histiocytosarcoma; 74 cases of the former condition and 36 of the latter were found in this group. Histioblastosarcoma was especially frequent among men and comprised 70% of male reticulosarcomas and 30% of female reticulosarcomas. During the development of these conditions, 27.7% of histiocytosarcoma patients and 2.6% of histioblastosarcoma patients showed cutaneous manifestations. Seventeen percent of histioblastosarcoma cases developed into leukemia, while none of the histiocytosarcoma cases developed into leukemia.

- 2109 PRELIMINARY OBSERVATIONS ON THE HISTOCHEMISTRY OF THE CELL SURFACE OF CARCINOMA OF THE CERVIX. (E.) Bradbury, S. (Dept. Human Anat., U. Oxford, England), G. Wiernik, E. A. Williams and R. H. Cowdell. *Brit J Cancer* 24(4):741-745, 1970.

Surface histochemistry of carcinoma of the uterine cervix and its response to radiation treatment was studied in squamous cell carcinoma human biopsies and one adenocarcinoma. The cell coat and intercellular matrix of the cervical carcinoma cell was rich in hyaluronic acid and did not contain any appreciable number of sulfate groups but was positive for sialic acid. The mucosubstances of the cell coat and intercellular matrix formula may be written C(G) mucosubstance; B 3.5; A 2.5 (0.6 M $MgCl_2$); T; S. Histochemical differences in the composition of the cell coat and intercellular matrix were not shown when comparing normal, carcinomatous and irradiated carcinomatous cervical tissue. It is obvious from these studies that this differs markedly from the trophoblast.

- 2110 THE STORAGE CELLS OF CHRONIC MYELOGENOUS LEUKEMIA. (E.) Lee, R. E. (U. Pittsburgh Sch. Med., Pa.) and L. D. Ellis. *Lab Invest* 24(4):261-264, 1971.

Bone marrow from patients with Gaucher's disease and chronic myelogenous leukemia was aspirated and prepared for electron microscopy. Leukemic cells were similar to Gaucher's disease cells under low magnification; however, under high magnification, the cytoplasmic sacs in the leukemic cells contained round, dense deposits peculiar to leukemic cells. Other linear deposits in the leukemic cells had a periodicity of 80-100 Å, and were composed of 2-20 parallel units. Gaucher cells contained cytoplasmic sacs comprising twisted tubes 300-400 Å in diameter with fibrillar walls. Ferritin particles were common in the storage cells of both leukemia and Gaucher's disease patients. Stored material in macrophage cells of leukemic patients was thought not to be cerebroside, or to be cerebroside in a different form from that in which it was found in cells from patients with Gaucher's disease.

- 2111 COMMENTS ON THE HISTOGENESIS OF MEDULLARY CARCINOMA OF THE THYROID WITH AMYLOID STROMA: REPORT OF 5 INSTANCES WITH ELECTRONMICROSCOPIC STUDY IN 2 CASES. (Fr.) Benatre, A. (C.H.R. Bretonneau, Tours, France), C. David and P. Jobard. *Arch Anat Path* 19(1):5-17, 1971.

Light microscopy of 5 medullary thyroid carcinomas with amyloid stroma revealed that initially the tumors were multicentric and perifollicular, with the tumor proliferation infiltrating the acini. Appearance of amyloid substance was relatively late and was completely lacking in more recent tumor nodules. Two cellular types were demonstrated by

electron microscopy: some rich in secretory granules and others with marked dilatation of cavities in the endoplasmic reticulum. Fluorescent and PAS studies suggest that after a secretory stage, tumor cells elaborate a pre-amyloid substance whose accumulation leads to depletion of cells. Since the parafollicular cells, which are precursors of medullary carcinoma are derived from the neural crest, it appears that cells other than mesenchymal cells can synthesize amyloid.

- 2112 BIOLOGICAL AND MORPHOLOGICAL CHARACTERISTICS OF MAMMARY TUMORS IN GR MICE. (E.) Van N. R. (Netherlands Cancer Inst., Amsterdam) and A. Dux. *J Nat Cancer Inst* 46(4):885-897, 1971.

The hormone dependency and growth of mammary tumors arising in GR mice was investigated in mice in 4 experimental categories: virgin mice, females bearing 1, 4 or 8 pituitary isografts in the kidney, ovariectomized mice treated with estrone, and force-bred mice. In addition, the progress of mammary tumors transplanted onto animals in these categories was observed. Mice in all groups developed mammary tumors with great frequency (84-100% incidence). Tumors appeared earlier in mice with pituitary grafts than in virgin mice; mice with 4 or 8 grafts developed tumors at an average age of 256-261 days, while mice with 1 graft developed tumors at an average age of 302 days. Ovariectomized mice treated with estrone also developed tumors earlier than did virgins; for bred mice developed tumors in 100% of the cases after the shortest latency (88 days of age) recorded for any group. Most tumors in the force-bred group were small and regressed after a few days. All tumors in virgin mice grew progressively; however, tumors in force-bred mice regressed after cessation of breeding and 3 of 10 tumors arising in mice with 1 pituitary graft regressed following ovariectomy and removal of the graft. Mammary tumors derived from virgin mice were transplanted to estrone-treated, estrone-and-progesterone-treated, and untreated mice with the result that 9 of 10 transplanted tumors grew in all mice, and were considered hormone-independent. Tumors from mice with 1 pituitary isograft were found on transplantation to be hormone-dependent, and tumors from ovariectomized mice treated with estrone were hormone-responsive and grew more efficiently in estrone-treated mice than in untreated castrated mice. Tumors derived from force-bred mice were hormone-dependent in 11 cases and were hormone-responsive in 2 cases. Most tumors arising in force-bred mice were classified morphologically as mammary tumor type P (pregnancy dependent), while most tumors arising in other groups were mammary adenocarcinomas types A and B. So-called "pale cell carcinomas" were also seen and were especially common in mice with pituitary isografts.

- 2113 BANDED STRUCTURES IN THE CONNECTIVE TISSUE OF LYMPHOMAS, LYMPHADENITIS, AND THYMOMAS (E.) Mollo, F. (Fac. Med. Surg., Turin, Italy) and G. Monga. *Virchow Arch Zellpath* 7(4):356-366, 1971.

Human lymph node and thymic tumors were examined electron microscopically; the thymic tumors were

granulomatous thymomas, and the lymph nodes were prepared from patients with Hodgkin's disease (24 specimens), reticulum cell sarcoma (6 specimens), lymphosarcomas (7 specimens), chronic lymphoid leukemia (3 specimens), acute leukemia (1 specimen) and nonspecific lymphadenitides (5 specimens). Distinctive banded structures in the connective tissue of lymph nodes were observed in 20 of the Hodgkin's disease cases, in 2 of the reticulum cell sarcoma cases, in 4 of the lymphosarcoma cases, in 1 of the nonspecific lymphadenitides and in both of the cases of granulomatous thymoma. Banded structures were prominent in Hodgkin's disease and thymoma specimens, and rarer in the other specimens. These structures were especially but not exclusively found in specimens showing fibrous or hyaline changes under the light microscope. Intercellular substances were sometimes seen in the specimens. Banded structures were usually ordered in a regular rhythmic manner, with a period of about 1000 Å; they were composed of interfibrillar ground substance and were sometimes associated with round areas of a similar dense ground material. The dense substance of the dark bands was similar to basement membrane material. In some cases, bands were abundant in the connective tissue surrounding small blood vessels. Collagen fibers, usually arranged in the conventional periodic pattern, and thick fibrillar structures were also seen.

- 2114 PROLIFERATION OF MICROBODIES AND SYNTHESIS OF CATALASE IN RAT LIVER: INDUCTION IN TUMOR-BEARING HOST BY CPIB. (E.) Reddy, J. (U. Kansas Med. Ctr., Kansas City) and D. Svoboda. *Amer J Path* 63(1):99-106, 1971.

Weanling male rats were given implants of an aflatoxin-induced hepatoma, an ethionine-induced hepatoma or an actinomycin-induced mesothelioma followed, after 8-12 wk of tumor growth, by a course of dietary ethyl- α -p-chlorophenoxyisobutyrate (clofibrate, CPIB). Liver catalase activity in animals bearing transplanted tumors was lower than in normals; catalase activity in normals measured 40 U/mg protein (mean) and catalase activity in animals bearing one or another of the 3 tumors used ranged from 13-19 U/mg protein. In rats given CPIB following tumor transplantation, catalase values increased and exceeded control values; catalase in CPIB-treated tumor-bearing rats ranged from 59-70 U/mg protein. Determination of the quantity of catalase protein in CPIB-treated tumor-bearing rats and in untreated tumor-bearing rats indicated that the content of catalase protein in the livers of normal rats and of tumor-bearing rats was significantly increased by treatment with CPIB.

- 2115 ULTRASTRUCTURAL STUDIES ON MONOCYTIC LEUKAEMIA. (E.) Freeman, A. I. (Roswell Park Mem. Inst., Buffalo, N.Y.) and L. J. Journey. *Brit J Haemat* 20(2):225-231, 1971.

Bone marrow cells from 7 patients with monocytic leukemia (Schilling type) or myelo-monocytic leukemia (Naegeli type) were examined under the electron microscope; monoblasts and myeloblasts were compared.

While myeloblasts showed regular rounded nuclei, monoblast nuclei were irregular with deep indentations or folds; bridges and blebs were common in monoblasts, rare or absent in myeloblasts. Chromatin condensation along the nuclear margin was seen in both cell types; however, myeloblast nuclei possessed nucleoli more often than did the nuclei of monocytes. Golgi apparatus was commonly seen in monoblasts, rarely in myeloblasts; Golgi bodies were often found in the indentations in the monoblast nucleus. Cytoplasmic volume was moderate in monoblasts and scanty in myeloblasts, as were fibrillar formations. Mitochondria, which were common in monoblasts, were scattered throughout the cytoplasm; mitochondria were uncommon in myeloblasts and, when found, were located in the polar areas of the cells. Cytoplasmic vesicles, vacuoles and pseudopodia, common or moderate in monoblasts, were rare or absent in myeloblasts.

- 2116 SPREAD OF TESTICULAR TUMOURS. (E.) Van Der Werf-Messing, B. (Rotterdam Radiother. Inst., Netherlands). *Clin Radiol* 22(1):125-132, 1971.

Of 279 cases of testicular tumors surveyed, including seminoma, malignant teratoma intermediate (MTI), MTI with seminoma (MTI/S), and malignant trophoblastic teratoma (MTT), seminoma showed the best survival rate (79% of patients were surviving at 5 yr after radiation therapy), and MTT showed the worst survival rate (no 5-yr survivors). Metastases were least prevalent in cases of seminoma (36% of cases had metastases), and most prevalent in MTT (100% of cases with metastases); seminoma usually metastasized to the lumbar glands, while MTT usually metastasized to other glands and/or to the intra-thoracic region (lung parenchyma or mediastinum). Lumbar recurrence in patients surviving 2 yr or more was found to be more frequent after orthovoltage radiation than after supervoltage radiation. Most patients with intra-thoracic lesions also showed hilar involvement, whatever the nature of their primary tumor. There was also a close relationship between the incidence of pulmonary lesions and lumbar metastases in all histological types of testicular tumors; liver metastases were also correlated with lumbar involvement. Seminoma was found to be the least aggressive condition and showed a comparatively slow rate of spread and high sensitivity to radiation therapy. MTT metastasized very rapidly and was relatively insensitive to radiation.

- 2117 ASSOCIATION OF PULMONARY TUBERCULOSIS AND CARCINOMA OF THE LUNG. (E.) Kreus, K-E. (U. Central Hosp., Helsinki, Finland), M. Hakama and E. Saxen. *Scand J Resp Dis* 51(4):276-289, 1971.

Of 6436 tuberculosis patients registered in Finland in 1958, 124 were diagnosed as having lung cancer between 1958-1963. Of 111 of these cases, there were 41 instances of misdiagnosed tuberculosis and 3 cases of misdiagnosed cancer, leaving 67 confirmed cases of lung cancer coincident with tuberculosis. In 57% of the confirmed cases, the lung cancer was epidermoid, and in 25% the cancer was either small cell or undifferentiated. Fifteen cancer patients

without tuberculosis and 20 cancer patients with tuberculosis showed roentgenographic signs of bronchial localization, including obstructive pneumonitis and atelectasis. In 19 patients with both cancer and tuberculosis, a unilateral change in the hilum was observed; this condition was seen in only 3 patients without tuberculosis. In 12 of 37 cases of unilateral tuberculosis the carcinoma was located in the region of the tuberculous lobe, indicating that the disease process does not determine the localization of the carcinoma. In more than half the cases of tuberculosis and lung cancer, the interval between diagnosis of tuberculosis and diagnosis of cancer was more than 3 years. The expected number of cases of lung cancer varied between 24 and 29, depending on the assumed risk of tuberculosis mortality, indicating that the risk of developing lung cancer among tuberculosis patients is higher than in the normal population. All nontubercular cancer patients, and at least 55 of the 67 tubercular cancer patients, were found to be heavy cigarette smokers.

- 2118 TUMOUR GROWTH IN NEMATODE-INFECTED ANIMALS.
(E.) Keller, R. (Dept. Derm., U. Zürich, Switzerland), B. Ogilvie and E. Simpson. *Lancet* 1(7701):678-680, 1971.

Female A-strain mice were infected with the nematode *Nippostrongylus brasiliensis* simultaneously with, 7 days after, or 7 days prior to inoculation with spontaneous murine mammary adenocarcinoma cells. Nematode-infected mice showed depressed tumor growth compared to uninfected mice; 30 days after inoculation of tumor cells, the mean tumor wt in nematode-infected mice ranged from 1.4-2.8 g, while the mean tumor wt in inoculated animals not infected with nematode was 4.7-5.2 g. Antilymphocyte serum did not increase the rate of tumor growth in uninfected mice, but it did prevent the inhibitory action of the nematode on tumor growth in infected mice. Osborne-Mendel rats were infected with nematode, and tumor cells (Walker 256 sarcoma) were injected on the same day or 5, 10 or 30 days later. Nematode infection did not affect the growth of tumors in rats infected on the same day that they were inoculated with tumor cells; tumor growth was inhibited 100% in rats inoculated on day 5 after parasite infection, and tumor growth was enhanced in rats inoculated 10 or 30 days postinfection. The enhancing effect could be transferred with antiserum from rats infected with the nematode only, suggesting that the tumor and the parasite have a common antigen.

- 2119 A SPECIFIC TYPE OF ORGANISM CULTIVATED FROM MALIGNANCY: BACTERIOLOGY AND PROPOSED CLASSIFICATION. (E.) Livingston, V. W. C. (U. San Diego, Calif.) and E. Alexander-Jackson. *Ann NY Acad Sci* 174(2):636-654, 1970.

The morphological and physiological characteristics of a cancer isolate were investigated, described and classified. The organisms were intermittently acid-fast and gram-variable, with rod forms predominantly

gram-positive and the L-forms gram-negative. Sensitivity was usually shown toward tetracycline, kanamycin, ampicillin, cephalothin, furacin and oleandomycin; however, isolates from the very ill were insensitive to these and resistance to penicillin, sulfa drugs, polymixin B, bacitracin and mycostatin was common; growth was inhibited by *Listeria* polyvalent O and mycoplasma antisera. The organisms are classified as: Order: *Actinomycetales*, Family: *Progenitoraceae*, Genus: *Cryptocides*, Species: *Cryptocides tumefaciens*, *Cryptocides sclerodermatis*, *Cryptocides wilsonii*, Variants: *hominis*, *rodentii*, *avii*, etc. They were able to grow aerobically, microaerophilically or anaerobically at 37° C and at room temperature, with acid production occurring from glucose and liquefaction of gelatin occurring slowly. A characteristic colony type on agar appeared as a "fried egg" and had the ability to invade both the cytoplasm and nucleus of vulnerable host cells or to remain in a latent non-invasive globoid or cyst form in the blood or other tissues in the presence of adequate body defenses.

- 2120 TOXIC FRACTIONS OBTAINED FROM TUMOR ISOLATES AND RELATED CLINICAL IMPLICATIONS.
(E.) Livingston, A. M. (U. San Diego, Calif.), V. W. C. Livingston and E. Alexander-Jackson. *Ann NY Acad Sci* 174(2):675-689, 1970.

The pathogenic effects of a microorganism belonging to the order *Actinomycetales* and the genus *Cryptocides* on HeLa cells in tissue culture has been studied utilizing various culture media and microscopic techniques. Inoculation of the whole culture in broth, even in relatively small doses, led to the death of the tissue culture. Cultures grown in the dark at room temperature yielded a dark red-brown zone of pigmentation. Yields of similar reddish-brown pigmented material were isolated from the urine of tumor-bearing patients in increasing amounts as the patient became terminally ill, and confirmatory cultures made from urine and blood of the same patients revealed the same pigmented material on extraction compared to the absence of such material in controls. In a strain of mice with known pulmonary tumor response, the incidence of pulmonary tumor was 20% among controls compared to 50.6% among mice receiving extract of a broth blood culture from a terminal breast cancer patient and 40% and 28% in 2 groups receiving an extract of urine from a terminal cancer patient. More selective methods of extraction and increased purification of the material are indicated to determine further the toxicity of the observed fractions.

- 2121 EXPERIMENTS WITH MAMMALIAN TUMOR ISOLATES.
(E.) Diller, I. C. (Inst. Cancer Res., Fox Chase, Philadelphia, Pa.) and A. J. Donnelly. *Ann NY Acad Sci* 174(2):655-674, 1970.

Isolation of pleomorphic organisms from blood and neoplasms of male and female mice of several different strains of known tumor incidence (C3H/HeN1cr, C57BL/6JN1cr, C58, ICR/Ha and ICR/albino) was attempted, and the effect of inoculation of such isolates into mice was studied. Of 100 randombred ICR/Ha mic

whose blood was sampled for the presence of organisms, 56 developed spontaneous tumors, and 49 of these yielded organisms from the blood at the time of death. Of the 44 non-tumor-bearing mice, 37 were negative throughout the study and the remaining 7 died of causes unrelated to cancer. Only 2 of the mice that produced tumors failed to yield the organism either from blood or tumor tissue. In male mice of the same strain, 19% tumor incidence was detected with an average of 14% positive findings in blood at death or sacrifice, while strain C58 mice showed an incidence of 95% lymphatic leukemia among both male and female animals with positive blood findings for organisms at 76% and 88%, resp. In C3H/HeNIcr and C57BL/6JNIcr strain female mice tumor incidence was 95% and 32.6%, resp., compared to 34% and 16%, resp., among males, while the occurrence of organisms in blood was 81% and 30% among females and 30% and 21% among males. The predominant forms of the organisms were coccoids and rods of various sizes, globoids, motile forms, mycelial forms and granules, some of which were filter-passing. All cultures reverted to the coccoid stage unless they were subcultured at frequent intervals; under phase microscopy, the coccoid forms were seen to elongate to form rods. *In vitro* inoculation into freshly isolated mouse embryo cells revealed intracytoplasmic organisms on the second day post-inoculation with penetration of the nucleus by 48 hr while *in vivo* inoculation into mice resulted in survival from 24 hr to 1 wk with resultant abscess formation, cellular breakdown and tissue necrosis. Inoculation of 50 ICR/albino mice under 72 hr of age with the S-180 organism resulted in tumors in 44% of the animals compared to 0% in controls. Since the pleomorphic acid-fast organisms can be cultured so consistently from malignant tissue, their presence may be related to the neoplasias.

2122 FOLLICULAR LYMPHOMA OF THE SPLEEN IN PATIENTS WITH HEPATOSPLENIC SCHISTOSOMIASIS MANSONI. (E.) Andrade, Z. A. (U. Bahia Sch. Med., Salvador, Brazil) and W. N. Abreu. *Amer J Trop Med Hyg* 20(2):237-243, 1971.

In a series of 863 patients with hepatosplenic schistosomiasis mansoni, 8 patients were found to have follicular lymphoma of the spleen. The spleens of all patients were markedly enlarged; numerous small rounded whitish nodules were usually found in the splenic pulp. Lymph nodes were enlarged in 7 of the cases of follicular lymphoma. Clinical histories of patients with follicular lymphoma were similar to the histories of patients with hepatosplenic schistosomiasis mansoni. In 1 patient, a reticulosarcoma developed as a supraclavicular mass. Splenic changes caused by schistosomiasis appears to predispose to follicular lymphoma.

2123 AMEBIC GRANULOMA AND ITS RELATIONSHIP TO CANCER OF THE CECUM. (E.) Camacho, E. (Fac. Med. U. Guadalajara, Jalisco, Mexico). *Dis Colon Rectum* 14(1):12-16, 1971.

Forty Mexican patients (23 males and 17 females) with amebic granuloma of the cecum and 20 patients (12 males and 8 females) with adenocarcinoma of the

cecum were surveyed. Twenty-three of the 40 cecal granuloma patients had granulomas in the transverse colon and sigmoid as well as in the cecum. Clinical symptoms of amebic cecal granulomas and cecal adenocarcinomas were similar, and it was thought that cecal granuloma may be a precancerous condition.

2124 MORPHOLOGICAL, BIOLOGICAL, AND IMMUNOLOGICAL STUDIES ON ISOLATES FROM TUMORS AND LEUKEMIC BLOODS. (E.) Seibert, F. B. (VA Ctr., Bay Pines, Fla.), F. M. Feldmann, R. L. Davis and I. S. Richmond. *Ann NY Acad Sci* 174(2):690-728, 1970.

Tissue from human tumors and blood from leukemic patients were examined for the presence of bacteria. Isolates from the tumors and leukemic blood older than 2 days showed marked pleomorphism and variability in staining capacity. With time these organisms became more acid-fast and repeated growth on 10% glycerol agar increased the amount of acid-fast bacteria in 2 strains. Electron microscopic examination revealed extremely heavy cell walls with at least 1 strain showing external processes resembling flagella. RBC in whole blood from a preleukemic patient incubated with isolates from leukemic patients were bombarded by bacteria, which resulted in their disintegration, and the white blood cells became engorged with the bacteria and were agglutinated. When plasma which contained freely moving bacteria was added to sterile plasma, agglutination occurred rapidly in contrast to the lack of agglutination when added to sterile normal human serum. Leukemic blood containing acid-fast particulate antigen particles reacted strongly and specifically with an antiglobulin to an organism isolated from a human breast adenocarcinoma and which cross-reacted with several antibodies to other organisms studied. Tumor tissues from ICR/albino mice that had developed tumors following injection of organisms also showed the presence of acid-fast particles which fluoresced when the tissues were treated with the labeled antiglobulin made to the organism injected.

2125 COMPARISONS BETWEEN MYCOBACTERIA AND ISOLATES FROM TUMORS AND LEUKEMIC BLOODS. (E.) Dunbar, F. P. (Trudeau Inst., Saranac Lake, N. Y.), E. Howard and R. Cacciatore. *Ann NY Acad Sci* 174(2):872-876, 1970.

Organisms which had not been identified as members of a single species ("unnamed strains") were isolated from a variety of sources including blood of leukemia, carcinoma and polycythemia patients, the blood of a sarcoma-bearing rat, breast tissue from a mouse possessing the Bittner factor, and saliva from a normal individual. The isolated organisms were grown in various media and subjected to testing to determine whether they were mycobacteria. Only 1 of 15 unnamed strains grew on agar or Lowenstein-Jensen medium when inoculated in the media in amounts of 0.001 mg; mycobacteria, in contrast, grew in these media almost without exception. When media were inoculated with larger amounts of unnamed factors, 26 of 35 unnamed strains produced growth. After repeated subcultures,

the unnamed strains were tested for susceptibility to 9 antimicrobial agents including streptomycin (33 of 38 cultures were susceptible), penicillin (34 of 38 strains were susceptible), gantrisin (20 of 38 strains were susceptible) and erythromycin (33 of 38 strains were susceptible). The unnamed strains were more susceptible to streptomycin and penicillin than were mycobacteria. Unnamed organisms did not reveal the acid-fast properties of mycobacteria, and were more motile than mycobacteria; furthermore, unnamed strains were more susceptible to drugs than was usual for mycobacteria.

- 2126 THE THYMUS GLANDS AND LYMPHOSARCOMA IN THE PIKE, *ESOX LUCIUS* L. (PISCES; ESOCIDAE) IN IRELAND. (E.) Mulcahy, M. F. (Dept. Zool., U. Coll., Cork, Ireland). *Bibl Haemat* 36:600-609, 1970.

Irish pike (*Esox lucius*) bearing spontaneous lymphosarcoma and pikes injected with tumor homogenates prepared from lymphosarcomatous pike were killed and their thymuses were examined. Of 11 lymphosarcomatous pike, 4 had thymic tumors and 7 had grossly normal thymuses. In thymic tumors, the neoplasms had replaced the thymus, and had invaded adjacent muscle tissue. In 5 lymphosarcomatous pike, the thymus was involuted. The most frequently involved sites in a series of 65 pike with lymphosarcoma were the upper and lower jaws, trunk, and thymus. Two pike were given injections of tumor homogenate from lymphosarcomatous pike; 56 days later, the thymus of 1 of the pike showed some distortion of its normal structure, and the other pike developed a lower jaw tumor with marked change in the thymus involving abnormal proliferation of lymphoid cells.

- 2127 ON THE STATE OF DEVELOPMENT OF THE RUDIMENTS OF THE MAMMARY GLANDS AND TEATS IN THE NEW-BORN MICE BELONGING TO 5 SELECTED LINES RAISED IN THE PARIS RADIUM HOSPITAL. (Fr.) Raynaud, A. (Inst. Pasteur, Paris, France), J. Raynaud, N. Dobrovolskaia, G. Rudali, N. Adamoff and J. Defoort. *Bull Cancer* 57(4):447-476, 1970.

Of 5 mouse lines maintained in the Paris Radium Hospital, 2 developed frequent spontaneous mammary carcinomas; one showed a less pronounced tendency to develop carcinoma, and 2 lines did not develop spontaneous mammary carcinomas. In the 2 lines which did not develop spontaneous mammary carcinomas, a large percentage of the male rats examined lacked mammary rudiments, probably as a result of testosterone secretion *in utero*. The highest incidence of mammary rudiments among male rats was seen in those lines having a strong tendency to develop mammary carcinomas. In the low-cancer lines, rudimentary mammae seldom remained connected with epidermis, whereas in the high-carcinoma incidence lines, mammary rudiments sometimes were attached to the epidermis. In female rats, elevated mammary rudiments were seen in rats from the high-cancer incidence lines and in the line with a lesser tendency to develop cancer.

- 2128 STUDIES ON THE RELATIONSHIP BETWEEN LYMPHOCYTOSIS AND BOVINE LEUKOSIS. (E.) Abt, D. A. (Sch. Vetr. Med., U. Pennsylvania, Philadelphia) R. R. Marshak, H. W. Kulp and R. J. Pollock, Jr. *Bibl Haemat* 36:527-536, 1970.

Cattle herds having a single member with leukosis and herds having several members with leukosis were surveyed for incidence of lymphocytosis; of 5,373 cows whose blood was sampled, 376 had persistent lymphocytosis, representing a lymphocytosis rate of 7%. In these herds, there were 147 cases of confirmed leukosis of which at least 42 occurred in animals identified as having persistent lymphocytosis prior to the onset of symptoms of leukosis. In 24 cattle herds ostensibly without leukosis, 174 animals were found to have lymphocytosis (4.2%). Studies of familial aggregations of lymphocytosis indicated that while the offspring of a particular animal generally have similar levels of absolute lymphocyte counts in a given herd, they may show different levels in other herds. In 1 herd, the offspring of a particular bull had elevated lymphocyte counts, while that bull's offspring residing in other herds had normal lymphocyte levels.

- 2129 PROGRESS ON TRANSMISSION OF BOVINE LYMPHOSARCOMA. (E.) Olson, C. (Dept. Vetr. Sci., U. Wisconsin, Madison), L. D. Miller, J. M. Miller and K. G. Gillette. *Bibl Haemat* 36:476-492, 1970.

In 45 cows with lymphosarcoma, lymph nodes of the pelvic region were involved in 30 cases, and tumors in the heart were found in 30 cases; the abomasum was invaded by tumor in 24 cases. In herd studies of cattle with lymphosarcoma, lymphocytosis was often but not always associated with lymphosarcoma and frequently followed inoculation of cattle with tumor cells. In cattle injected with antigenic tumor lymph nodes, signs of a mild anaphylactic reaction were observed in 2 of 5 cases. Attempts to transmit lymphosarcoma by means of tumor cell suspensions at various ages and following X-irradiation were generally unsuccessful. An increase of lymphocyte nuclear projections was found regularly in lymphosarcomatous cattle and in cows with lymphocytosis. C-type particles were found in the majority of lymphosarcomatous cattle in 1 experiment; calves inoculated with lymphosarcoma material also showed C-type particles. It was not clear if the C-type particles were viruses or if they were causally related to the development of lymphosarcoma. Lymphocytosis was found to be more common and C-type particles were more often observed in cattle of a relatively advanced age.

- 2130 STUDIES ON LYMPHOCYTOSIS IN REGIONS OF HIGH AND LOW INCIDENCES OF BOVINE LEUKOSIS AND BABESIOSIS. (E.) Hugoson, G. (Natl. Vetr. Inst., Stockholm, Sweden). *Bibl Haemat* 36:537-543, 1970.

Hematological examination of Swedish cattle herds revealed that within a region of high bovine leukosis incidence the frequency of lymphocytosis was

higher than in regions of low leukosis incidence, the frequencies of leukosis in high and low lymphocytosis areas being 16.8 and 0.7%, resp. In the high leukosis region, the frequency of lymphocytosis in herds without a collective history of leukosis was 14.3%, while the frequency of lymphocytosis in herds with a history of leukosis was 19.4%. Herds with a single case of leukosis and herds with 2 or more cases of leukosis (multiple-case herds) showed similar frequencies of lymphocytosis. No cases of babesiosis, and no vaccinations against babesiosis, were found in cattle herds in an area of low leukosis incidence. The frequency of lymphocytosis in animals in herds vaccinated against babesiosis was lower than the frequency of lymphocytosis among cattle in herds without a babesiosis history and lower than that in unvaccinated herds in which babesiosis had occurred; however these differences were not statistically significant.

2131 CANINE MAST CELL LEUKEMIA. (E.) Post, J. E. (New York St. Vetr. Coll., Cornell U., Ithaca), F. Noronha and C. G. Rickard. *Bibl Haemat* 36:425-429, 1970.

Mast cell leukemias arising in Beagle dogs were transmitted through 15 generations by serial transfer of viable cells; during these passages, the latent period for mast cell tumor appearance decreased from 27-28 days to 6-8 days. Cell-free transmission of the tumor was not successful until the 8th passage, after which cell-free transmission was usually successful. In an additional 24 passages of the tumor through 24 generations, tumor transmission with cells was successful in 93 of 114 inoculated puppies. While adult dogs resisted tumor induction, dogs as old as 3 months developed tumors upon inoculation with fresh tumor cells. Cell-free transmission of mast cell leukemias was successful in 65 of 171 puppies; cell-free ascitic or pleural fluid and bone marrow produced higher incidences of tumors than plasma or tissue culture fluid. Transmission of tumor with ultrafiltrates produced few tumors. Mast cell leukemia induced by cellular or cell-free filtrates were similar to the spontaneous disease from which the inducing preparations were derived. C-type virus particles were found in tumor cells, but they were rare.

2132 SERIAL CELLULAR TRANSMISSION OF CANINE LYMPHOMA. (E.) Moldovanu, G. (Sloan Lettering Inst. Cancer Res., New York, N. Y.). *Bibl Haemat* 36:416-424, 1970.

Canine lymphosarcoma was passed through 15 transplant generations of mongrel dogs that had been irradiated (100 r) shortly after birth by two s.c. inoculations of lymphosarcoma cells (10^5) in the nape of the neck; inoculation was usually followed by the development of a local lymphoid tumor within 9-19 days which spread to bone marrow, liver, lungs and kidneys. When lymphosarcoma cells were injected into beagle dogs, lymphosarcomas failed to develop for 5 months, at which time 1 dog died with generalized visceral lymphoma. Another beagle died at 7 months with a large lymphosarcoma, and a third showed a small

regressing tumor. In subsequent transplant generations of beagles, local tumors remained comparatively small, thymuses were enlarged and infiltrated by lymphosarcoma, and metastases were found in brain and cerebellum. Lymphosarcoma cells from beagles were injected into irradiated adult guinea pigs, and 7 of 9 animals developed fibrosarcoma at the injection site. The tumor material from the guinea pigs produced lymphosarcoma in 1 puppy.

2133 PROSPECTIVE STUDY OF DOG BITE AND CHILDHOOD CANCER. (E.) Norris, F. D. (California St. Dept. Publ. Hlth., Berkeley), E. W. Jackson and E. Aaron. *Cancer Res* 31(4):383-386, 1971.

The number of deaths from leukemia and lymphoma among 49,239 children bitten by dogs in the Los Angeles area was less than the expected number of leukemia-lymphoma deaths when the time elapsed between bite and death was less than 4 yr. When the interval between bite and leukemia-lymphoma death was 4 or more yr, there were 5 deaths observed compared to 1.67 expected among children aged 10-14-yr-old. Standardized leukemia-lymphoma mortality ratios for the 10-14-yr-old age group rose about 3-fold following an interval of 4 or more yr after the bite. However, similar increases in risk were not observed in children of other age groups. There was no reason to believe that children bitten by dogs are at a significantly higher risk of leukemia-lymphoma development than unbitten children.

2134 MICROPROBE ANALYSIS OF LOCALIZED CONCENTRATIONS OF METALS IN VARIOUS HUMAN TISSUES. (E.) Carroll, K. G. (Forsyth Dent. Ctr., Boston, Mass.), J. E. Mulhern, Jr. and V. L. O'Brien. *Oncology* 25(1):11-18, 1971.

Metallic concentrations in human thyroid, lung, breast, stomach, colon, ovary, and rectal benign and malignant tissue were evaluated using electron microprobe analyzer techniques. High metal concentrations of Ca, Ti, Cr, Fe, Ni, Cu and Zn were found in all tissue specimens. The frequency of occurrence of metallic concentrations in malignant tissue, which exhibited many more metal localizations, appeared to be greater than in normal tissue. However, the data are too limited at this time to conclude that there are significant differences in metal content between normal and pathological tissue, or between similar tissues taken from different individuals.

2135 THE AETIOLOGY OF PRIMARY LIVER CANCER IN THE BANTU. (E.) Torres, F. O. (Miguel Bombarda Hosp., Lourenco Marques, Mozambique), I. F. H. Purchase and J. J. Van der Watt. *J Path* 102(3):163-169, 1970.

Liver biopsy specimens taken from a Bantu population in Mozambique at the time of an epidemic of acute hepatitis were from 112 cases of infections hepatitis and 89 cases of "toxic liver damage," and 278 random biopsies including 128 specimens of primary

liver cancer. In view of the high incidence rate of liver cancer among the Bantu (98.2 cases/100,000 population for males) biopsies were compared with material taken from the livers of rats manifesting malignant change and other pathology as a result of maintenance on a diet of sterigmatocystin (10, 20 or 100 mg/kg for 6 months followed by 15, 30 or 150 mg/kg for a further 6 months). Biopsies of human specimens of primary liver cancer showed well-differentiated primary hepatocellular carcinomas with limited bile-duct proliferation and well-developed tumor nodules adjacent to hyperplastic nodules. The pathological picture associated with primary liver cancer was similar to that associated with toxic liver damage and to that observed in livers of rats on the carcinogenic diet. On this basis, it was suggested that liver damage in the Bantu was related to a food-borne toxin, possibly a mycotoxin.

- 2136 INDUCTION OF MURINE LEUKEMIA WITH HUMAN NEOPLASTIC TISSUE. (E.) Dosne Pasqualini, C. (Nat'l. Acad. Med., Buenos Aires, Argentina), F. Saal, A. Pavlovsky and S. L. Rabasa. *Bibl Haemat* 36:304-311, 1970.

One-month-old BALB/c mice were inoculated in the spleen by trocar with cells from hypertrophied human lymph nodes of patients with neoplastic diseases including hemocytoblastoma, fibrosarcoma, Hodgkin's disease, chronic lymphoid leukemia, lymphosarcoma and granuloma. Half of 139 inoculated mice developed leukemias with latencies of 10-46 days; lymphosarcomas and reticulosarcomas as well as true leukemias developed. Leukemias developed in 100% of mice given inocula of hemocytoblastoma, in 88% of mice given fibrosarcoma inocula, and 80% of mice given Hodgkin's disease inocula. Inocula consisting of cultured Burkitt's lymphoma cells EBI and P3J produced leukemias in 30% and 83% of mice, resp. Long term leukemias were observed after 18-20 months in 35% of mice inoculated with human lymphoma cells, including cells from patients with Hodgkin's disease, acute leukemia and hemocytoblastoma. Long-latency leukemias occurred with especially high incidences in mice treated with cells which had produced short-latency leukemias in other mice. Apparently, a mechanism of leukemogenesis is present in BALB/c mice which is activated by inocula of human lymphoma cells.

- 2137 CANCER OF THE CERVIX IN THE PRESENCE OF MULTIPLE TUMORS. (Ger.) Tatra, G. (2nd U. Women's Clin., Vienna, Austria) and A. Kratochwil. *Wien Med Wsch* 121(11):202-204, 1971.

Examination of case records of 324 patients with fatal carcinoma of the cervix revealed an incidence of 4.6% (15) with primary multiple tumors. Histological examination demonstrated the presence of multiple cancer formation in various tissues other than the cervix, including bronchus, bone, kidney, corpus uteri, ovary, gallbladder, stomach, rectum and colon. It is noteworthy that mammary carcinoma

as a secondary cancer was never observed in this clinic. Surprisingly, the second cancer was clinically recognized in only 2 cases, and these only when it was too late to consider treatment. In general, secondary and tertiary cancer sites were identified only at autopsy. Therapy with multiple carcinoma was considered largely unsuccessful.

- 2138 DE-NOVO BRAIN TUMOURS IN RENAL-TRANSPLANT RECIPIENTS. (E.) Schneck, S. A. (U. Colorado Med. Ctr., Denver) and I. Penn. *Lancet* 1(7707):983-986, 1971.

Among 5000 kidney transplant recipients and 170 heart transplant recipients on record, there were 24 instances of the development of mesenchymal tumors in homograft recipients; of these 24 mesenchymal tumors, 11 involved the brain. In 8 of the 11 instances of brain tumors arising following organ transplantation the brain was the only organ involved; in 3 cases tumors were found in the cervical lymph nodes, lung and/or skin in addition to the brain. The age of organ recipients developing brain tumors ranged from 14-46 yr; 7 of the patients were male. In 6 cases, the transplant donor was a blood relative of the recipient. All patients developing brain tumors were treated with prednisone and azathioprine, and 3 of the patients were given anti-lymphocyte globulin. The tumors included 9 reticulum cell sarcomas, 2 unclassified lymphomas, and 1 Kaposi's sarcoma. Tumors developed from 5.5-46 months after transplantation. Brain tumors appeared sooner after transplantation than did non-cerebral mesenchymal or epithelial tumors.

- 2139 COMPARATIVE MORPHOLOGIC STUDY OF BRONCHOALVEOLAR CANCER AND PULMONARY ADENOMATOUS CHANGES IN MAN. (E.) Uzunov, P. (Visshia Med. Inst. Sofia, Bulgaria). *Nauch Tr Vissh Med Inst Sofia* 49(3):83-93, 1970.

Tissues from the lungs of 18 patients with bronchoalveolar carcinoma and from 36 cases of pulmonary adenomatous changes (mainly children) were examined microscopically. Lumina of varying sizes which were similar to alveoli were seen in preparations of both bronchoalveolar cancer and pulmonary adenomatous changes. In both conditions, the lumina were covered with epithelial cells which contained neutral and acid mucopolysaccharides. In bronchoalveolar cancer the epithelial cells showed papillary outgrowths directed towards the lumina, while in adenomatous changes, papillary outgrowths were rare. Cellular atypism and metastases were observed in bronchoalveolar cancer tissues, but not in tissues from patients with adenomatous change. While mucopolysaccharides were found in the lumina of bronchoalveolar cancer tissues, mucopolysaccharides were only rarely found in the lumina in tissues from patients with adenomatous change. Collagens and reticular fibers in bronchoalveolar cancer cells were coarse, while in tissues undergoing adenomatous change they were slender. Apparently, pulmonary adenomatous changes represent a non-neoplastic proliferative regenerative process.

2140 A CASE REPORT OF GIANT VESICAL CALCULUS ASSOCIATED WITH SQUAMOUS METAPLASIA. (*Jap.*) Toyahara, N. (Med. Sch. Osaka City U., Japan) and S. Ono. *Acta Urol Jap* 16(8):384-392, 1970.

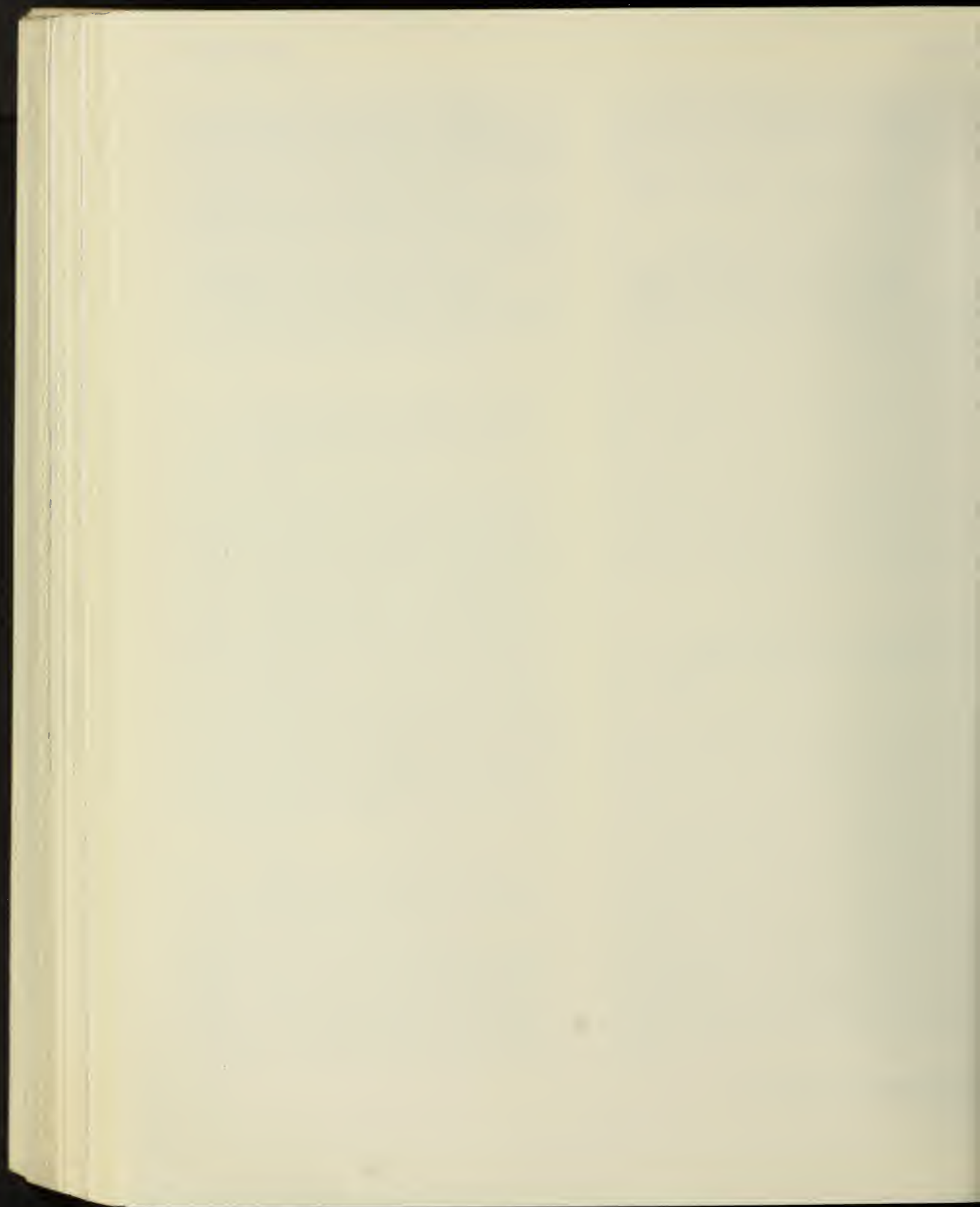
2141 URETERAL LEUKOPLAKIA: REPORT OF A CASE. (*Jap.*) Tokuhara, M. (Shuto Hosp., Japan). *Acta Urol Jap* 16(7):331-333, 1970.

2142 ULTRASTRUCTURAL INVESTIGATIONS OF ACID CARBOHYDRATES IN THE CYTOPLASMIC MEMBRANE OF BLOOD LYMPHOCYTES IN HUMANS AFFECTED BY LYMPHOID LEUKEMIA. (*Fr.*) Calman, F. (Hosp. St. Louis, Paris, France), J. L. Binet and J. Bernard. *C R Acad Sci* 272(6):884-885, 1971.

2143 BONE LESIONS AND DISTRIBUTION OF METASTASES IN AN EXPERIMENTAL PLASMACYTOMA OF BALB/c MICE (HIPA TUMOR). (*Ger.*) Büsser, E. (Inst. Path. Anat. U. Zurich, Switzerland), G. Pedio and J. R. Rüttner. *Path Microbiol* 36(4):243-255, 1970.

2144 GROWTH AND SPREAD OF EHRlich ASCITES CARCINOMA OF THE MOUSE IN THE CHICK EMBRYO. (*Ger.*) Gonzenbach, P. (Inst. Path. Anat., U. Zurich, Switzerland). *Path Microbiol* 36(4):200-214, 1970.

2145 PRIMARY FIBROSARCOMA OF LUNG AND DIABETES MELLITUS. (*E.*) Turner, M. A. (Western Infirm., Glasgow, Scotland) and C. H. W. Horne. *Brit J Surg* 57(9):713-715, 1970.



AUTHOR INDEX

ARON, E.
 2133
 BAURREA, C.
 1928
 BELEV, G.I.
 2003
 BERDEEN, E.R.
 1806
 BREU, W.N.
 2122
 BT, D.A.
 2128
 DAMOFF, N.
 2127
 DAMSON, R.
 1802
 DEE, R.R.
 1843
 DEKUNLE, A.
 1779
 EIKENS, B.
 1819
 HEARN, M.J.
 1969
 HMED, M.
 1965
 HSTROEM, L.
 2015
 KERVALL, K.
 1912
 LEKSANDROV, S.N.
 1845, 1863*, 1864*
 LEANDER-JACKSON, E.
 1946, 2119, 2120
 LEN, P.
 2050
 LTHOFF, J.
 1813
 LVARES, A.P.
 1805
 MES, R.P.
 1925
 NASTASIU, GH.
 1844
 NDERER, F.A.
 1909
 NDERSON, K.M.
 1990
 NDRADE, Z.A.
 2122
 NGHILERI, L.J.
 2085
 NTON-LAMPRECHT, U.
 2026
 FFEL, C.A.
 1758*
 RCHER, V.E.
 1859
 RCHIBALD, F.M.
 2068
 COS, J.C.
 1731
 MBRECHT, B.H.
 1778
 AHINA, M.
 1771
 ERBACH, O.
 1859

AVILA, L.
 1882
 BADER, J.P.
 1940
 BAKER, M.
 1903
 BAKER, R.
 1903
 BALDAUF, W.
 1879
 BALDELLOU, A.
 1756*
 BALL, J.K.
 1896
 BALLESTA, F.
 1756*
 BALLIS, M.E.
 2083
 BALUDA, M.A.
 1942
 BANERJEE, M.R.
 1802
 BANWASCH, P.
 1818, 2073
 BARAHONA, H.H.
 1918, 1919
 BARANSKA, W.
 1931
 BARBAN, S.
 1953
 BARBIERI, D.
 1906
 BARCLAY, M.
 2068
 BAREKAT, A.A.
 2041
 BARRILLIOT, L.
 1963*
 BARSKI, G.
 1906, 1908
 BASELGA, J.
 1757*
 BASKAR, J.F.
 1977
 BASSIN, R.
 1933
 BASSIR, O.
 1779
 BASTERIS, B.
 2004
 BASU, M.
 1958
 BEARD, D.
 1735, 1890
 BEARD, J.W.
 1735, 1890
 BEASLEY, J.N.
 1915
 BEAUDREAU, G.S.
 1892, 1893, 2082
 BELEHRADEK, J., JR.
 1906
 BENATRE, A.
 2111
 BENDA, P.
 1991
 BENEDICT, W.F.
 2098

BENNETT, M.H.
 1849
 BENSO, L.
 2021*
 BENYESH-MELNICK, M.
 1881, 1885, 1923
 BERNARD, J.
 2142*
 BERNSTEIN, I.D.
 1992
 BERTALANFFY, F.D.
 1782
 BERUMEN, L.
 2108
 BERWICK, L.
 1865
 BHIDE, S.V.
 2081
 BIBBO, M.
 2045
 BIERWOLF, D.
 1956
 BIETZEL, W.
 1932
 BINET, J.L.
 2142*
 BIRD, C.C.
 1846
 BISHOP, D.
 1798
 BISHOP, J.M.
 1941, 1943
 BISWAL, N.
 1881
 BLACK, H.S.
 1856
 BLAIR, P.B.
 1927
 BLOOM, E.T.
 1986
 BLUEFARB, S.M.
 1723
 BNEDER, E.
 1956
 BOCK, F.G.
 1793
 BOGER, E.
 1795
 BOLOGNESI, D.P.
 1887
 BOOTHE, A.D.
 1875
 BOURGEOIS, C.H.
 1777
 BRADBURY, S.
 2109
 BRAENDSTRUP, O.
 2102
 BRAWERMAN, G.
 2071
 GRODEY, R.S.
 1975, 2044
 BROWN, C.D.
 2098
 BROWN, D.W.
 2063
 BRUCHER, J.M.
 2080

- BRUNSWIG, J.P.
1885
- BUCK, C.A.
1939, 1957
- BUDER, E.
1851
- BUECHER, J.
1823
- BUERKLE, G.
1819
- BUESSE, E.
2143*
- BULAY, O.M.
1797
- BULHILLER, H.
1879
- BUNNEY, W.E.
1835
- BURDON, R.H.
2097, 2100
- BURG, C.
1987
- BURGER, C.L.
1894
- BURKITT, D.P.
2040
- BURTON, A.C.
1728
- BUSSE, V.
1766
- BUSSMANN, J.F.
2029
- BUTLER, W.H.
1807, 1808, 1809
- BYVOET, P.
2056
- CACCIATORE, R.
2125
- CAFFIER, H.
1911
- CALDWELL, B.V.
1993
- CALMAN, F.
2142*
- CAMACHO, E.
2123
- CAMAIN, R.
2004
- CAPPELAERE, P.
1742
- CARO, W.A.
1723
- CAROLI, J.
1780
- CARROLL, K.G.
2134
- CARROZZA, G.
2033*
- CASALS, J.
1995
- CHANDAVIMOL, P.
1777
- CHANDRA, S.
1925
- CHANG, E.
2072
- CHAPDINET, Y.
1963*
- CHARNEY, J.
1929
- CHERRY, C.P.
1790
- CHIARUGI, V.P.
2025
- CHIECO-BIANCHI, L.
1970
- CHIRIGOS, M.A.
1933
- CHOLON, J.J.
1869
- CHOPRA, H.C.
1870
- CHRISTOFFERSEN, P.
2102
- CHU, C.T.
1972
- CHYLE, M.
1836*, 1837*
- CHYLE, P.
1836*, 1837*
- CILIEVICI, O.
1844
- CIOBANU, Z.
1979
- CITOLER, P.
1822
- CLARK, W.R.
1961
- CLARKE, D.H.
1995
- CLARKSON, B.D.
1996
- CLIFFORD, P.
1973
- COLLAVO, D.
1970
- CONNEY, A.H.
1796
- CONRAD, P.A.
1961
- COOKE, K.O.
1880
- COOMBS, M.M.
1763
- CORNEFERT-JENSEN, F.
1876
- CORNICK, G.
1913
- CORRIN, B.
2103
- CORY, J.G.
1907
- COWDELL, R.H.
2109
- CUNNINGHAM, D.D.
1960
- DABHOLKAR, R.D.
2036
- DALLENBACH-HELLWEG, G.
2027
- DANIEL, M.D.
1917, 1919
- DANIEL, M.R.
2075
- DAO, T.L.
1791
- DAUNE, M.
1772
- DAVID, C.
2111
- DAVIES, J.N.P.
2019
- DAVIES, R.E.
1860
- DAVIES, R.F.
1806
- DAVIS, J.M.G.
1852
- DAVIS, R.L.
2124
- DE ASUA, F.J.
1928
- DEENEY, A.O.
2082
- DEFENDI, V.
1954
- DEFOORT, J.
2127
- DE HARVEN, E.
1898, 1975
- DEN, H.
1958
- DENT, P.B.
1997
- DE RUDDER, J.
1759*
- DESHPADE, V.A.
2042
- DE-THE, G.
1922
- DIANZANI, M.U.
1725
- DIEHL, V.
2015
- DILLER, I.C.
2121
- DI MARCO, A.T.
1989
- DJORDJEVIC, J.
1850
- DMOCHOWSKI, L.
1866, 1938, 1976
- DOBROVOLSKAIA, N.
2127
- DODD, D.C.
2012
- DOLL, F.
2043
- DONAWICK, W.J.
2012
- DONNELLY, A.J.
2121
- DONNER, L.
1921
- DONNER, M.
1987
- DORN, C.R.
2039
- DOSNE PASQUALINI, C.
2136
- DOUGHERTY, R.M.
1964
- DOURMASHKIN, R.R.
2007, 2008

OWNS, W.G.
1995
OYEN, G.
2080
RAKE, B.J.
1723
RECHSLER, H.J.
1822
UNBAR, F.P.
2125
UNKEL, V.C.
1882
URBIN, C.G.
1778
UTCHER, R.M.
1870, 1873
UTTA, S.K.
1877
UTZ, W.
2041
UX, A.
2112
YADKOVA, A.M.
1947
BERT, P.S.
1933
CKNER, R.
1900
DWARDS, F.
1888
ILBER, F.R.
1880, 1984
ISEN, H.N.
2006
LGJO, K.
2059
LLIS, L.D.
2110
NDO, H.
1746
NGELHARDT, N.V.
2003, 2004
NOMOTO, N.
1827
RNBERG, I.
1971
SBER, H.
1993
ULITZ, H.
2020*
ULITZ, M.
2020*
EVANS, D.L.
1915
EVERETT, M.A.
1855
FABRIKANT, J.I.
2051
FABRIZIO, D.P.A.
1925
FANSHIER, L.
1941, 1943
FARAS, A.
1943
FELDMANN, F.M.
2124
FENYVES, A.
1979

FERBER, E.
2057
FERGUSON, D.B.
1868
FILIPE, M.I.
2069
FINKEL, G.C.
1776
FISCHER, H.
2057
FISCHINGER, P.J.
1934
FLICKINGER, J.T.
1899
FLOHE, L.
1819
FLOREY, M.
1903
FLOYD, R.
1923
FOURNIER, E.
1834
FOX, T.O.
1952
FRABLE, W.J.
2105
FRANCESCHI, C.
1989
FRANK, H.
1909
FRANKLIN, R.M.
1912
FRANKS, L.M.
2099
FRAYSSINET, C.
2072
FRAZIER, M.E.
1838
FREEMAN, A.I.
2115
FREEMAN, M.A.R.
1853
FRIEND, C.
1897, 1898
FRYE, F.L.
2044
FUCHS, R.
1772
FUERSTENBERG, H.S.
2029
FUJIMOTO, Y.
1861*
FUJINAGA, S.
1938
FUJIOKA, S.
1950
FUKUSHIMA, M.
1983
GALKOVSKAYA, K.F.
1845, 1863*, 1864*
GALLAGHER, R.E.
1962
GALLIPPI, G.
2033*
GALLO, R.C.
1950, 1962, 2089,
2091

GANÉ, N.F.C.
1849
GARAPIN, A.C.
1941, 1943
GARFINKEL, H.A.
1830
GARLAND, M.R.
1770
GARVEN, E.V.
2097
GAZDAR, A.F.
1932
GEERING, G.
1975
GELDERBLOM, H.
1909
GELETA, J.N.
1778
GENTILE, J.M.
1899
GERARD-MARCHANT, R.
2108
GERBER, P.
1883, 1884
GERGELY, L.
1971
GILBERT HOLLAND, J.
1897
GILLETTE, K.G.
2129
GINSBERG, H.S.
1913
GLASSER, R.
1923
GLICK, M.C.
1939, 1957
GLUCKSMANN, A.
1790
GMINDER, J.
1812
GOENZCOEL, E.
1921
GOERLICH, M.
1751*
GOFMAN, J.W.
2095, 2101
GOLDFEDER, A.
1842
GOLDMAN, L.I.
1792
GONANO, F.
2025
GONZENBACH, P.
2144*
GOODWIN, F.K.
1835
GOOR, R.S.
1953
GOTO, S.
1784
GOUSSEV, A.I.
2003, 2004
GRACE, J.T., JR.
1882, 1886
GRAEF, W.
1747
GRAESSMAN, M.
2077

GRAESSMANN, A.
 2077
 GRAFFI, A.
 1956
 GRAFFI, I.
 1956
 GRAHAM, C.E.
 1769, 1804
 GRANGE, J.
 1949
 GREEN, M.
 1911
 GREEN, N.M.
 2008
 GREENBLATT, M.
 1817
 GREENWALD, P.
 2019
 GROSS, L.
 1734
 GROSSMAN, R.A.
 1777
 GROSSO, G.
 2087
 GROUPE, V.
 1910
 GRUENSTEIN, M.
 1792
 GRUNBERGER, D.
 2090
 GRUNDMANN, E.
 1767
 GUARINI, G.
 2021*
 GUBAREVA, A.V.
 1845, 1863*, 1864*
 GUEST, G.B.
 1873
 GUETTNER, J.
 1764
 GUNVEN, P.
 1973
 GURDA, M.
 2010, 2023*
 GUTMANN, H.R.
 1773
 HADDAD, J.R.
 1898
 HAJDUKOVIC, S.
 1848
 HAKAMA, M.
 2117
 HAMMER, R.F.
 1877
 HAMPEL, K.E.
 1766
 HAMPERL, H.
 2035*
 HANNA, M.G., JR.
 2001
 HARAN-GHERA, N.
 1968
 HARD, G.C.
 1807, 1808, 1809
 HARDY, W.D.
 2044
 HARDY, W.D., JR.
 1975, 1977

HARMAN, J.W.
 1786
 HARTENSTEIN, R.
 1812
 HARVEY, J.J.
 1935
 HAY, D.
 1895
 HAYAHARA, N.
 2140*
 HAYASHI, K.
 1765
 HEATH, C.W., JR.
 2096
 HEATH, J.C.
 1853
 HENLE, G.
 1973
 HENLE, W.
 1973
 HENNINGS, H.
 2059
 HERBST, A.L.
 1831
 HERTZ, R.
 2076
 HILDEMAN, W.H.
 1986
 HILLEMANN, M.R.
 1961
 HIRAI, K.
 1954
 HIRONO, I.
 1765
 HIRSCHMAN, S.Z.
 1733
 HOBBS, J.R.
 1737
 HOD, I.
 1930
 HOKAMA, A.
 1983
 HOLMES, E.C.
 1984, 1985
 HOMBURGER, F.
 1795
 HORN, M.
 1764
 HORNE, C.H.
 2145*
 HOROSZEWICZ, J.S.
 1882
 HOSSFELD, D.K.
 1730
 HOWARD, E.
 2125
 HOWARD, E.B.
 1838, 1841
 HOYER, B.H.
 1884
 HSIUNG, G.D.
 1920
 HUEBNER, R.
 1871
 HUEBNER, R.J.
 1888, 1977
 HUGOSON, G.
 2130

HUHN, D.
 2020*
 HUNT, R.D.
 1917
 HURLBURT, J.F.
 1857
 ICHIMURA, H.
 1826
 IDA, N.
 1905
 IGAKI, T.
 1826
 IKAWA, Y.
 1905, 1937
 IMASHUKU, S.
 2064
 INCH, W.R.
 1998
 IOACHIM, H.L.
 1865
 ISHIBASHI, A.
 2106
 ISHIKAWA, Y.
 1983
 ISHIZAKI, R.
 1890
 ISOK, M.E.
 1814
 ITO, T.
 1839, 1840
 IUDICELLO, P.
 2021*
 JACKSON, E.W.
 2133
 JACKSON, J.
 1941
 JACKSON, T.A.
 1843
 JACOB, R.M.
 2021*
 JACQUEMONT, R.
 1949
 JAFFE, B.M.
 2006
 JAITLEY, S.B.
 1763
 JANIS, R.
 2017
 JANNERS, M.Y.
 2050
 JARRETT, O.
 1895
 JENSEN, E.M.
 1925
 JEREB, B.
 2015
 JOBARD, P.
 2111
 JOHNSEN, D.O.
 1777
 JOHNSON, E.M., J.
 2064
 JOHNSON, W.C.
 1860
 JOHNSTONE, C.
 2012
 JOURNEY, L.J.
 2115

UCHAU, M.R.
1799
UHL, E.
2102
UMINER, B.
1727
UNGSTAND, W.
1764
USSAWALLA, D.J.
2042
APLOW, L.S.
1920
APULER, A.M.
1774
ARASAKI, S.
2061
ASUGA, T.
2106
ATO, N.
1784
ATO, T.
1861*
AWAKAMI, T.G.
1874
AWAMURA, A., JR.
1972
AY, S.
2105
EARN, F.
1798
EEBLER, C.M.
2045
EEN, P.
1781
ELLEN, J.A.
1990
ELLER, R.
2118
ESSLER, I.I.
1724
HOKHLOVA, M.P.
2048
IEFER, G.
1775
IESSLING, A.A.
1892, 1893, 2082
IM, C.S.
1817
IMURA, M.
1810
IRSTEN, W.H.
1936
IRTANE, J.S.
2038
IT, S.
1951
ITAGAWA, T.
1784
IVILAAKSO, E.
2070
EIN, G.
1739, 1971, 1973
EIN, M.G.
1859
INGE, O.
2073
OPFER, U.
2013

KNIGHT, S.C.
1996
KOIZUMI, J.
2104
KOJIKI, M.
1983
KOMABA, M.
1983
KONO, S.
2140*
KOPROWSKI, H.
1931
KORB, J.
1837*
KOREN, H.S.
2057
KOROL, W.
1925
KRAKOFF, I.H.
2083
KRAMARSKY, B.
1926
KRARUP, T.
1787
KRASNANSKAYA, P.N.
1833
KRATOCHWIL, A.
2137
KREUS, K.E.
2117
KROH, H.
2087
KRSMANOVIC, V.
2071
KRUEGER, F.W.
1762
KULLMANN, R.
1775
KULP, H.W.
2128
KUNIMOTO-MIYATA, S.
1784
KUNTZMAN, R.
1805
KUNZE, E.
2024
KURIHARA, T.
1826
KURIMURA, T.
1951
KUSCHNER, M.
1859
KUZNETSOV, O.K.
1947
LABROSSE, E.H.
2064
LACKNER, A.
1766
LAGERLOEF, B.
1889
LAGERON, A.
1780
LAIRD, H.M.
1895
LANDO, D.
1759*
LONDON, J.C.
1872, 1974

LANE BROWN, M.M.
2093
LANGE, J.
1909
LANGLOIS, A.J.
1735, 1890
LANZEROTTI, R.
2005
LARSON, C.
1903
LARSON, V.L.
1877
LARSON, V.M.
1961
LASFARGUES, E.Y.
1926
LASKOV, R.
2005
LAUSCH, R.N.
1982
LAVAPPA, K.S.
1828
LEE, R.E.
2110
LEE, S.Y.
2071
LEECH, J.B.
1965
LEFKOWITZ, S.S.
1981
LEINIKKI, P.
1755*
LEONG, B.K.J.
1761
LEONG, J.A.
1941
LEVI, M.M.
2000
LEVINE, A.J.
1952
LEVINE, L.
2089
LEVINSON, W.
1941, 1943
LEVY, C.C.
2074
LEWIS, A.M., JR.
1980
LEWIS, R.T.
1885
LIBBY, P.R.
1791
LICHTENBERGER, E.
2035*
LIKHACHEV, A.YA.
1816
LILLY, F.
1904
LIN, P.S.
1873
LINDUP, R.
1849
LIPKIN, M.
2076
LIVINGSTON, A.M.
2120
LIVINGSTON, V.W.C.
2119, 2120

LOEWE, K.R.
 2029
 LOFT, H.
 1787
 LOH, A.
 1796
 LOONEY, W.B.
 2050
 LOUIS, J.B.
 1825
 LOURIA, D.B.
 1776
 LOUSSOUARN, J.
 2031*
 LOZANO, R.
 1757*
 LUCCA, A.
 2055*
 LUDWIG, H.
 1881
 LYNCH, T.P., JR.
 2068
 MACEK, M.
 1885
 MAC FARLAND, H.N.
 1761
 MAC MILLAN, D.S.
 2093
 MADON, E.
 2021*
 MAGEE, P.N.
 1820
 MAHALEY, M.S., JR.
 2018
 MAHER, B.C.
 1894
 MAJOR, I.R.
 1806
 MAK, S.
 1914
 MALAN, L.B.
 1974
 MALATHI, V.G.
 1901
 MALMGREN, R.A.
 1880
 MALMQUIST, W.A.
 1875
 MANKOWSKI, Z.T.
 1801
 MANN, J.R.
 2060
 MANOCHA, S.L.
 1769
 MANZKE, E.
 1862*
 MARCUS, D.M.
 2017
 MARINI, M.
 2025
 MARK, J.
 2092
 MARKHAM, P.D.
 1942
 MARSHAK, R.R.
 1876, 2012, 2128
 MARTENS, J.G.
 2012

MARTIN, J.E.
 2012
 MARTIN, P.
 1781
 MARUYAMA, K.
 1976
 MASEK, V.
 1800
 MASSEYEFF, R.
 2004
 MATHE, G.
 2108
 MATSUYAMA, M.
 1829
 MATVEYCHUK, YA.D.
 1794
 MAYO, A.A.
 2050
 MC CALL, M.G.
 2049
 MC CARTER, J.A.
 1896
 MC COY, J.
 1936
 MC CREDIE, J.A.
 1998
 MC DONNELL, J.
 1943
 MC DONOUGH, S.K.
 1975, 2044
 MC GOVERN, V.J.
 2093
 MC MILLAN, M.
 2103
 MEDINA, D.
 1789, 1802
 MELENDEZ, L.V.
 1917, 1918, 1919
 MELLGREN, J.
 2052
 MELLON, J.G.
 2050
 MELNICK, J.L.
 1924
 MENEZES, J.
 1955
 MERANZE, D.R.
 1792
 MERKER, H.
 1753*
 MESROBIAN, A.Z.
 1788
 MESSER, J.
 1821, 1991
 METTLER, N.E.
 1995
 MEYERS, P.
 1964
 MICHELSON, A.M.
 1774
 MIKULIK, F.M.
 1969
 MILLER, E.C.
 1827
 MILLER, E.S.
 2085
 MILLER, J.A.
 1827

MILLER, J.M.
 2129
 MILLER, L.D.
 2129
 MINEI, S.
 2104
 MINKLER, J.L.
 2095, 2101
 MIRAND, E.A.
 1902
 MIWA, T.
 1765
 MIZUNO, D.
 1784
 MOHR, U.
 1813
 MOLDOVANU, G.
 2132
 MOLLO, F.
 2113
 MOLONEY, J.B.
 1910
 MONGA, G.
 2113
 MONROE, J.H.
 1883
 MONTESANO, R.
 1820
 MONTGOMERY, P.O.
 1825
 MOORE, A.L.
 1874
 MOORE, D.
 1878
 MOORE, D.H.
 1926, 1929
 MOORE, E.G.
 1945
 MOORE, G.E.
 1996
 MORBIDELLI, R.
 2055*
 MORGAN, H.R.
 1948
 MORGAN, L.G.
 2043
 MORGENROTH, V.H.
 2064
 MORI, H.
 1765
 MORRIS, H.P.
 2050, 2056
 MORROW, R.H.
 1973
 MORTON, D.L.
 1880, 1984
 2016
 MOSCOVICI, C.
 1891
 MULCAHY, M.F.
 2126
 MULHERN, J.E., J.
 2134
 MULLIGAN, R.M.
 1740
 MUNN, R.J.
 1874

MURPHY, D.L.
1835
MAGATA, C.
1745
MAIK, S.N.
2036
MAKAJIMA, K.
1951
MAKASHIMA, S.
1994
MAKAZAWA, I.
2058
MAMBA, M.
1824
MAZERIAN, K.
1916
METTESHEIM, P.
2001
MCG, T.
1770
MICOLA, P.
1760*
MIELSEN, S.L.
1821
MIEPELT, N.
1762
MIGRO, N.
2021*
MIKULIN, A.
1850
MISKANEN, E.
2070
MORDQUIST, J.
1855
MORONHA, F.
2131
MORRBY, K.
2052
MORRIS, F.D.
2133
MORARA, T.
1887
MURBRIEN, V.L.
2134
MUSCHNER, A.
1741
MURCONNOR, T.E.
1934
MUSILVIE, B.
2118
MUSHA, Y.
1905
MUSKUMA, S.
1784
MUSHTA, A.
1826
MUSKUBO, S.
1999
MUSLD, L.J.
1975, 1977
MUSPIN, J.L.
1894
MUSSON, C.
2129
MUSSON, R.L.
1855

MOMURA, G.A.
2083
MONEILL, B.J.
2011
MOTOOLE, C.
2015
MOZHAN, M.L.
1782
MONTRAND, M.
2108
PALMER, D.L.
2063
PAPANEEK, M.
1837*
PARISER, R.J.
1960
PARKHOUSE, R.M.E.
2007, 2008
PARROTT, J.C.W.
1782
PARSONS, J.
1911
PASS, F.
2017
PATOCCA, F.
1836*
PATTERSON, L.T.
1915
PAUL, J.S.
1825
PAVLOVSKY, A.
2136
PEASE, P.
1726
PEDIO, G.
2143*
PENN, I.
2138
PENNELLI, N.
1970
PERK, K.
1930
PERMAN, V.
1877
PEROCCO, P.
1989
PETERS, J.H.
1758*
PETO, R.
1798
PETRAKIS, N.L.
2094
PETTERSSON, U.
1912
PEYDRO OLAYA, A.
1785
PHILIPSON, L.
1912
PIENTA, R.J.
1969
PIKULA, B.
1850
PILCH, Y.H.
1988
PILLINGER, D.J.
2088

PIRRO, G.
2025
PISTER, L.
1909
PLAMENAC, P.
1850
PLENERT, W.
1738
POLLOCK, R.J., JR.
2128
PONG, R.S.
1744
PONOMAR'KOV, V.I.
2107
PONZONE, A.
1760*
PORTER, I.H.
2098
POSKANZER, D.C.
1831
POSSEHL, E.A.
2082
POST, J.E.
2131
POTMESIL, M.
1842
POTTER, M.
1736
POULSEN, H.
2102
POWELL, L.C., JR.
1832
PREUSSMAN, R.
1762
PRODI, G.
1989
PURCHASE, I.F.H.
2135
RABASA, S.L.
2136
RABES, H.
1812
RABIN, H.
1919
RAHN, I.
1851
RAKHMANIN, P.P.
2048
RAMMING, K.P.
1988
RANADIVE, K.J.
2081
RANDELIA, H.P.
2036
RAO, P.R.
1967
RAPP, F.
1982
RAPP, H.J.
1992
RASKAS, H.
1911
RAUSCHKOLB, E.W.
1856
RAWCLIFFE, R.M.
1858

RAWLS, W.E.
 1924
 RAYKHLIN, N.T.
 2030
 RAYNAUD, A.
 2127
 RAYNAUD, J.
 2127
 REDDY, J.
 2114
 REDMAN, L.W.
 1770
 REESE, H.W., JR.
 1761
 REUSS, W.
 1818
 RICH, M.A.
 1907
 RICHARD, M.H.
 1949
 RICHARDS, J.F.
 1770
 RICHMOND, I.S.
 2124
 RICHTERS, A.
 2079
 RICHTERS, V.
 2079
 RICKARD, C.G.
 1976, 2131
 RIDDICK, D.H.
 2091
 RIDDLE, P.
 1959
 RIFKIND, D.
 2063
 RIGBY, C.C.
 2099
 ROBINSON, H.
 2037
 ROBINSON, H.L.
 1944
 ROBINSON, W.S.
 1944
 ROE, F.J.C.
 1798
 ROM, W.
 2027
 ROMANENKO, A.M.
 2028
 ROSEMAN, S.
 1958
 ROSSI, G.B.
 1898
 ROTHMAN, I.K.
 1901
 ROWE, W.P.
 1980
 RUDALI, G.
 2127
 RUETTNER, J.R.
 2143*
 RUOSLAHTI, E.
 2002
 RUSSELL, D.H.
 2074
 RUSSELL, W.J.
 1854

RYTOEMAAA, T.
 2070
 SAAL, F.
 2136
 SACCOMANNO, G.
 1859
 SAHEKI, R.
 2086
 SAIDI, F.
 2041
 SAKAI, T.
 1803
 SALAK, D.
 2050
 SANDBERG, A.A.
 1730
 SANDER, J.
 1819
 SANDERS, C.L.
 1843
 SANDOR, T.
 2032*
 SANDRITTER, W.
 1775

 SANO, M.
 2067
 SARMA, P.S.
 1871, 1888, 1977
 SARRAZIN, G.
 1771
 SATO, J.
 1824
 SATO, K.
 2086
 SATO, T.
 1983
 SAUNDERS, R.P.
 1859
 SAWICKI, W.
 1931
 SAXEN, E.
 2117
 SAYED, B.A.
 2038
 SCAMPS, R.A.
 2011
 SCHAEFER, W.
 1909
 SCHARFF, M.D.
 2005
 SCHAUER, A.
 2024
 SCHAUF, V.
 1936
 SCHEPERS, G.W.H.
 1748, 1749, 1750
 SCHER, W.
 1897
 SCHERF, H.R.
 1815
 SCHIDLOVSKY, G.
 1965, 1985
 SCHILLER, A.L.
 1821
 SCHILLING, G.
 1805

SCHLOM, J.
 1878, 1910
 SCHLUMBERGER, J.R.
 2108
 SCHMAEHL, D.
 1815
 SCHMIDEK, H.H.
 1821
 SCHNECK, S.A.
 2138
 SCHNEIDER, R.
 2039
 SCHNYDER, U.W.
 2026
 SCHRAMM, T.
 1851, 1956
 SCHULSON, N.G.
 1857
 SCHULTZ, A.M.
 1958
 SCHULZ, G.
 1766
 SCHWARZMANN, W.
 1780
 SEIBERT, F.B.
 2124
 SEIDEL, E.H.
 1885
 SENDA, H.
 2084
 SEPPELAE, M.
 2002
 SEYMOUR, R.J.
 1832
 SHALKOP, W.T.
 1778
 SHANK, R.C.
 1777
 SHARPE, C.A.B.
 2093
 SHELLABARGER, C.J.
 1847
 SHERR, C.J.
 2009
 SHERWIN, R.P.
 2079
 SHETH, N.A.
 2081
 SHIMKIN, M.B.
 1792
 SHIMOJO, H.
 1978
 SHIPOVA, L.JA.
 2003
 SHKLAR, G.
 1788
 SHOPE, R.E.
 1995
 SHOPE, R.E., JR.
 1877
 SHUBIN, A.S.
 2107
 SIEGLER, R.
 1729
 SIGLER, P.B.
 1913
 SILBER, R.
 1901

SIMMS, E.S.
2006
SIMPSON, E.
2118
SIMPSON, J.S.
2060
SINKOVICS, J.G.
1969
SKIPSKI, V.P.
2068
SLATTERY, S.M.
1965
SMITH, G.H.
1927
SMITH, J.K.
1776
SMITH, J.L.
2083
SMUCKLER, E.A.
1783
SNODGRASS, M.J.
2001
SNYDER, S.P.
1872
SOEHNER, R.L.
1938
SOMEDA, K.
1991
SOOFI, G.S.
1894
SORENSEN, D.K.
1877
SPAHN, G.
1933
SPEIZER, F.E.
2043
SPIEGELMAN, S.
1878
SRINIVASAN, D.
2090
SRINIVASAN, P.R.
2090
SRIVANNABOON, S.
2014
SRIVATANAKUL, P.
1981
STANDFAST, S.J.
2042
STEEVES, R.A.
1900, 1902
STEINHOFF, D.
1767
STELLWAGEN, R.H.
2078
STENBACK, W.A.
1868
STENGLEIN, B.
1879
STENHOUSE, N.S.
2049
STICKL, H.
1879
STILL, W.J.S.
2105
STJER, SWAERD, J.
2015

STOCK, C.C.
2068
STOCK, N.D.
1873, 1876
STOCKS, P.
2047
STOKER, M.G.P.
1959
STRANDBERG, B.
1912
STREETER, A.M.
2011
STRICKLAND, P.
1849
STRYCKMANS, P.
1732
STUART, J.
2060
STUMPHIUS, J.
2046
SUBBUSWAMY, S.G.
2066
SUGANO, H.
1937
SUTHERLAND, R.M.
1998
SUZUKI, H.
1829
SVOBODA, D.
2114
SWANSON, S.A.V.
1853
SWEET, W.H.
1991
SYDOW, G.
1811
SZANTO, J.
1909
TAKANO, T.
1784
TALAL, N.
1932
TANDY, R.K.
2095, 2101
TAPER, H.S.
2060
TAROCCO, R.P.
1760*
TATRA, G.
2137
TAYLOR, D.O.
2039
TAYLOR-PAPADIMITRIO, J.
1959
TEMIN, H.M.
1945
TERAS, L.E.
1814
TEXIER, J.L.
2108
THEILEN, G.H.
1872, 1874
THEODOSSIOU, A.
1818
THOMAS, C.
1822, 1823

THOMPSON, M.
1770
THOMSON, S.
1902
THORNEYCROFT, I.H.
1993
TILGEN, W.
2026
TILLSON, S.A.
1993
TING, R.C.Y.
1950, 1962
TOKUHARA, M.
2141*
TOMINAGA, T.
1791
TOMKINS, G.M.
2078
TORRES, F.O.
2135
TRAHAN, E.
1985
TRAININ, Z.
2013
TREGER, A.
1795
TRENTIN, J.J.
1868
TREPPEL, F.
1754*
TRIDENTE, G.
1970
TRKULA, D.
1951
TRONCALE, F.
2076
TRUJILLO, J.M.
1969
TSUCHIYA, E.
2106
TSUIKI, S.
2086
TUMILOWICZ, J.J.
1869
TURKEVICH, N.M.
1794
TURKINGTON, R.W.
2062
TURNER, H.C.
1888
TURNER, M.A.
2145*
TURNER, W.
1933
TUROWSKA, B.
2023*
TURPIN, J.
2031*
UEBERHORST, P.J.
1871
UHR, J.W.
2009
ULFELDER, H.
1831
UNGLAUB-LEISTEN, I.
1879

URBACH, F.
 1860
 USHIJIMA, R.
 1903
 USHIJIMA, R.N.
 1838
 UZUNOV, P.
 2139
 VAHERI, A.
 1755*
 VAHRSON, H.
 2034*
 VAISHNAV, V.P.
 2038
 VAN DER MAATEN, M.J.
 1875
 VAN DER WATT, J.J.
 2135
 VAN DER WERF-MESSING, B.
 2116
 VAN DE WIELE, R.L.
 1743
 VAN HOOSIER, G.L., JR.
 1868
 VAN NIE, R.
 2112
 VAN VUNAKIS, H.
 2089
 VEPREK, L.
 1890
 VERMIGLIO, G.
 2033*
 VERNON, L.
 1888
 VIALE, E.
 2087
 VIALE, G.L.
 2087
 VIANNA, N.J.
 2019
 VIRELLA, G.
 2007
 VOLEGOV, A.I.
 2022*
 VONKA, V.
 1923
 WAGNER, G.
 2053*

WAGNER, R.
 1815
 WALKER, J.E.
 1758*
 WARREN, L.
 1939, 1957
 WATANABE, M.
 1966
 WATANBE, K.
 1771
 WEBER, A.F.
 1877
 WEBER, G.H.
 1892, 1893, 2082
 WEINBERGER, M.
 1792
 WEINSTEIN, I.B.
 2090
 WEISS, D.W.
 1927
 WELCH, R.M.
 1796
 WELLER, W.
 1768
 WEPSIC, H.T.
 1992
 WETTELAND, P.
 2054*
 WETZEL, R.
 1851
 WHANG-PENG, J.
 1871, 1883
 WHITWELL, F.
 1858
 WIED, G.L.
 2045
 WIERNIK, G.
 2109
 WILKINSON, R.
 2088
 WILLIAMS, E.A.
 2109
 WILLIS, R.A.
 1846
 WIMBERLY, I.
 1885
 WINE, S.S.
 1860
 WOGAN, G.N.
 1744

WOLFE, L.G.
 1872
 WOOD, W.C.
 2016
 WOODING, W.L.
 1777
 WU, S.Y.
 1783
 YAGIHASHI, H.
 1983
 YAKOVLEVA, L.A.
 1867
 YAMAGATA, S.
 2058
 YAMAHA, T.
 1771
 YAMAMOTO, H.
 1978
 YANG, C.S.
 1972
 YERGANIAN, G.
 1828
 YOKOYAMA, T.
 1784
 YOSHIKURA, H.
 1937
 YUSHOK, W.D.
 2065
 ZALDIVAR, R.
 2037
 ZARIDZE, D.G.
 2030
 ZBAR, B.
 1922
 ZENKER, N.
 2064
 ZEVE, V.
 1871
 ZIEGLER, J.L.
 1973
 ZIEVE, F.J.
 1773
 ZINTL, F.
 1738
 ZIVY, P.
 1834
 ZUR HAUSEN, H.
 1752*

SUBJECT INDEX

- ACETOXY-2-ACETYLAMINOFLUORENE
 - DNA, BINDING (1772)
 - DNA, POLYNUCLEOTIDES (1774)
- ADRENAL GLAND
 - ESTROGEN-DEPENDENT CARCINOMA, RNA AND DNA METABOLISM (1770)
- AFLATOXIN
 - B1, REYE'S SYNDROME, TOXIC REACTION IN MONKEYS (1777)
 - BEAGLE, LIVER CHANGES (1778)
 - DNA, RNA, REVIEW (1744)
 - HEPATIC CHANGES, ENDOPLASMIC RETICULUM, MITOCHONDRIAL ATPASE, RATS (1780)
 - SWAZILAND, LIVER CARCINOMA (1781)
- AGE
 - CARCINOMA, HORMONES, ANTIGENICITY (1740)
 - NEW ZEALAND MICE, MURINE SARCOMA VIRUS, TUMOR REGRESSION (1932)
 - TUMOR, EPIDEMIOLOGY, REVIEW (1725)
- AIR POLLUTION
 - LUNG CANCER MORTALITY, AUSTRALIAN IMMIGRANTS (2049)
- ALKYLATING AGENT
 - CHLORAMBUCIL, BUSULPHAN, BONE MARROW CELL PROLIFERATION (2070)
- AMINOAZOBENZENE
 - N,N-DIMETHYL-4-AMINOAZOBENZENE, LIVER CELL NUCLEI RNA POLYMERASE, OTHER DERIVATIVES, RAT (1783)
- ANTIBODY
 - ANTISARCOMA, HUMAN SARCOMA, VIRUS (1880)
 - 4-AZOGUINOLINE-1-OXIDE, 4-NITROQUINOLINE-1-OXIDE (1994)
 - EPSTEIN-BARR VIRUS, BURKITT'S LYMPHOMA (1973)
 - EPSTEIN-BARR VIRUS, BURKITT'S LYMPHOMA, TAIWAN MONKEY (1972)
 - HETEROLOGOUS ANTIGLIOMA "CARRIER", GLIOMAS, HUMAN (2018)
 - MAMMARY GLAND TUMOR, 7,12-DIMETHYLBENZ(A)ANTHRACENE (1990)
 - TITERS, EPSTEIN-BARR VIRUS, MACAQUE MONKEYS (1974)
- ANTIGEN
 - ADENOVIRUS TYPE 12, HELA CELL (1981)
 - CARCINOMA, HORMONES (1740)
 - CELL-SURFACE, SARCOMAS, HUMAN (2016)
 - CHICKEN FEATHER FOLLICLES, MAREK'S DISEASE HERPESVIRUS (1965)
 - CHORIOCARCINOMA, PLACENTA, KIDNEY (2014)
 - COMPLEMENT FIXATION, HEMAGGLUTINATION REACTION, MURINE LEUKEMIA VIRUSES (1909)
 - GROUP SPECIFIC, FELINE LEUKEMIA VIRUS (1975), 1977)
 - HUMAN WART (2017)
 - METHYLCHOLANTHRENE SARCOMA, TRANSPLANTATION, GUINEA PIG (1985)
 - SARCOMA 180, 15 VIRUSES (1995)
 - SPLEEN, RETICULUM CELL SARCOMAS, AGE, MICE (2001)
- SV40, ADENOVIRUS, 2-SV40 HYBRIDS (1980)
- TRANSPLANTATION, HUMAN, MOUSE LEUKEMIA VIRUS, ETIOLOGY, MONONUCLEOSIS (1738)
- TRANSPLANTATION, TUMOR GLYCOPROTEINS, REVIEW (1758)*
- TUMOR, ANTI-TUMOR REACTIONS (1754)*
- ULTRAVIOLET IRRADIATION, VIRUS (1978)
- ASBESTOS
 - DUST, LUNG GRANULOMAS, MICE, HAMSTERS (1852)
 - DUST EXPOSURE, PULMONARY FUNCTION, OCCUPATIONAL EXPOSURE (1857)
 - ENGLAND, PLEURAL MESOTHELIOMA (1858)
 - NETHERLANDS SHIPYARDS, MESOTHELIOMA (2046)
- ASCITES
 - EHRlich TUMOR, LIVER ARGINASE, UREA CYCLE ENZYME (2067)
 - SARCOMA 180, MRNA, POLYSOME (2071)
 - TUMOR CELLS, ADENINE NUCLEOTIDE, MICE (2065)
- ASTROCYTOMA
 - N-NITROSOMETHYLUREA, GLIOBLASTOMA, RAT (1991)
 - N-NITROSOMETHYLUREA, GLIOMAS, RAT (1821)
- AZATHIOPRINE
 - CHROMOSOMAL MUTATIONS, HUMAN LEUKOCYTES, OXIMAZON (1766)
- AZO DYE
 - HEPATOMA, ULTRASTRUCTURE, RAT (1785)
- BACILLUS CALMETTE-GUERIN
 - MYCOBACTERIUM BOVIS, FRIEND DISEASE VIRUS, IMMUNITY (1903)
- BACTERIA
 - MALIGNANCY, BACTERIAL CARCINOGENESIS (1726)
 - ROUS SARCOMA VIRUS (1946)
 - TUMORS, LEUKEMIA (2124)
- BENZO(A)PYRENE
 - FIBROSARCOMA, CYCLOPHOSPHAMIDE, HYDROCORTISONE, RAT LIVER (1815)
 - HYDROXYLATION, HUMAN PLACENTA, TOBACCO (1799)
 - METABOLISM OF CARCINOGEN, CIGARETTE SMOKE (1796)
 - OCCUPATIONAL EXPOSURE, COKE OVEN (1800)
 - OCCURRENCE, SYNTHESIS, MAN, ANIMAL (1747)
 - SKIN, NEUTRAL FRACTION, CIGARETTE SMOKE, MICE (1798)
 - TUMOR, LUNG, SKIN, MOUSE FETUS (1797)
- BIS(CHLOROMETHYL) ETHER
 - CHRONIC INHALATION, LUNG ADENOMAS, MICE (1761)
- BLADDER
 - EPITHELIAL TUMOR, DARK CELLS, HISTOCHEMISTRY, HUMANS (2028)
 - TRANSITIONAL CELL TUMOR, CHROMOSOME PATTERN, HUMAN (2099)
 - TUMORS, DNA, B-GLUCURONIDASE, HUMAN (2084)

- URINARY, DIBUTYLNITROSAMINE TUMORS, RAT (2024)
 URINARY, SQUAMOUS METAPLASIA, GIANT VESICAL CALCULUS (2140)*
- BONE
 LESIONS, MURINE PLASMACYTOMAS, METASTASES (2143)*
 TRAUMA, WHOLE BODY IRRADIATION, OSTEOGENIC SARCOMA, MOUSE (1863)*
 TUMORS, MOLONEY MURINE SARCOMA VIRUS, HARVEY MURINE SARCOMA VIRUS (1938)
- BONE MARROW
 CHLORAMBUCIL, BUSULPHAN (2070)
 HYDROGEN TRANSPORT, LEUKEMIA, HUMAN (2060)
 X-IRRADIATION, MITOTIC ABERRATIONS, RAT (1844)
- BRAIN
 BLOOD BARRIER, TUMORS, METHYLNITRO-SOUREA, RAT (1822)
 MALIGNANCIES, ACID AND ALKALINE NUCLEASE (2080)
 MESENCHYMAL TUMORS, ORGAN TRANSPLANT PATIENTS (2138)
 TUMORS, T-RNA, R-RNA (2087)
- BURKITT'S LYMPHOMA
 ANTIBODIES, EPSTEIN-BARR VIRUS (1973)
 EPSTEIN-BARR VIRUS (1886)
 EPSTEIN-BARR VIRUS, TUMOR MEMBRANE ANTIGENS (1970)
 HERPES SIMPLEX VIRUS, GROWTH (1923)
 IODODEOXYPRIDINE, CYTOSINE ARABINOSIDE (1971)
 NASOPHARYNGEAL CARCINOMA, HERPES-TYPE VIRUS (1922)
- CARCINOGENESIS
 THEORY, CONTACT INHIBITION, CELL PROLIFERATION (1728)
- CARCINOGENICITY
 HUMAN MALIGNANCY, E16 CHROMOSOME (2095)
 4-NITROQUINOLINE-1-OXIDE, REVIEW (1746)
 POLYPHENOLS, TOBACCO, MOSAIC VIRUS (1836)*
- CELL
 DARK, URINE BLADDER TUMOR, HUMANS (2028)
 MYOEPIHELIAL, ROLE IN BENIGN AND MALIGNANT TUMORS (2035)*
- CENTRAL NERVOUS SYSTEM
 TUMORS, BLOOD BRAIN BARRIER, METHYLNITROSOUREA, RAT (1822)
- CERVIX
 ATYPIA, PREVALENCE AND INCIDENCE, COMPUTERIZED STUDY (2045)
 CANCER, MULTIPLE TUMORS, THERAPY (2137)
 CANCER, RISK IN PAROUS INDIAN WOMEN, EPIDEMIOLOGY (2042)
 CARCINOMA, ANTIBODIES, HERPESVIRUS TYPE 2 (1924)
 CARCINOMA, MUCOSUBSTANCE, HUMAN (2109)
 ESTRADIOL, DIETHYLSTILBESTEROL, EPITHELIAL CHANGES, MONKEYS (1769)
 HERPES, CANCER, REVIEW (1755)*
 MALIGNANCY, ORAL CONTRACEPTIVE,
- DEPO-MEDROXYPROGESTERONE ACETATE (1832)
 SQUAMOUS CELL CARCINOMA, TS ANTIGENS, OVARIAN CYSTADENOCARCINOMA (2000)
- CHEMICAL CARCINOGEN
 INDUSTRIAL, PULMONARY TUMORS, RODENTS, PRIMATES, REVIEW (1749)
 INDUSTRIAL, TUMOR MORPHOLOGY, LUNG TUMORS (1750)
 MONONITROQUINOLINES, ELECTRONIC STRUCTURE, HUCKEL (1826)
 SYNTHESIS, 15,16-DIHYDRO-7-METHYL-CYCLOPENTA(A)PHENANTHRENE-17-ONE (1763)
- CHILDREN
 CANCER, EPIDEMIOLOGY, ITALY (2055)*
 LEUKEMIA, DOG BITE (2133)
 NEOPLASMS, SEROLOGICAL STUDY (2021)
- CHLORPROPAMIDE
 LIPOMA (1830)
- CHROMATIN
 METHYLASE, HISTONE (2097)
- CHROMOSOME
 ABERRATION, VACCINIA VIRUS, HUMAN LYMPHOCYTES (1879)
 DOWN'S SYNDROME, BLOOM'S SYNDROME, LEUKEMIA, REVIEW (1756)*
 E16, HUMAN MALIGNANCY (2095)
 HERPES SIMPLEX VIRUS, L CELLS, HEP2 (1921)
 HUMAN MALIGNANCY, ENVIRONMENTAL CARCINOGEN (2101)
 KARYOTYPE STUDIES, CHLOROLEUKEMIA, GRANULOCYTIC LEUKEMIA, RAT (1803)
 LEUKEMOGENESIS, GROSS VIRUS, MICE (1904)
 LONG ACROCENTRIC MARKER, SOLID TUMORS, MALIGNANT EFFUSIONS (2098)
 METAPHASE, DNA, EPSTEIN-BARR VIRUS (1881)
 MITOSIS, RNA, DNA (2072)
 MUTATIONS, AZATHIOPRINE, METAPHASES, OXIMAZON (1766)
 PATTERN, TRANSITIONAL CELL TUMOR, HUMAN (2099)
 PHILADELPHIA, CHRONIC MYELOCYTIC LEUKEMIA (1730)
 PHILADELPHIA, LEUKEMIA (1753)*
- COBALT ALLOY
 WEAR PARTICLES, PROSTHESIS, TUMOR INDUCTION (1853)
- COLON
 PROLIFERATING CELLS, NEOPLASTIC LESION, NUCLEIC ACID METABOLISM (2076)
- CYCASIN
 HAMSTER LIVER TUMORS, NEWBORN AND ADULT HAMSTERS (1765)
- CYCLAMATE
 CYCLOHEXYLAMINE, URINARY EXCRETION IN HUMANS (1771)
- CYCLOHEXYLAMINE
 SODIUM CYCLAMATE, URINARY EXCRETION IN HUMANS (1771)
- CYTOGENETICS
 LYMPHOID CELL LINES, EPSTEIN-BARR

VIRUS (1884)
 TOTOXIC REACTION
 MASTOCYTOM CELLS, PHOSPHOLIPID
 METABOLISM (2057)
 IRY PRODUCT
 CONSUMPTION, BREAST CANCER MORTALITY,
 REGIONAL VARIATIONS IN ENGLAND
 (2047)
 PO-MEDROXYPROGESTERONE ACETATE
 CERVICAL MALIGNANCY, ORAL CONTRA-
 CEPTIVE (1832)
 BENZOPYRENE
 TRICAPRYLIN, ADENOMA, LIMONENE, MOUSE
 (1795)
 BUTYLNITROSAMINE
 URINARY BLADDER TUMORS, ALKALINE
 PHOSPHATASE, RAT (2024)
 3'-DICHLORO-4,4'-DIAMINO-DIPHENYL-ETHER
 CARCINOGENICITY, AUDITORY CANAL, RAT
 (1767)
 ETHYLNITROSAMINE
 GLUCOSE-6-PHOSPHATASE, HORMONE, LIVER,
 RABBIT, RAT (1814)
 LACTATING HAMSTERS, TUMOR INDUCTION
 IN OFFSPRING (1813)
 LIVER CANCER, IMMUNOSUPPRESSION, RAT
 (1815)
 RENAL TUMORS, PARTIAL HEPATECTOMY,
 RAT (1812)
 TRANSPLACENTAL EFFECT, LIVER NECROSIS,
 PNEUMONIA, RAT (1811)
 TRANSPLACENTAL EFFECT, LUNG ADENOMA,
 MOUSE (1816)
 DIMETHYLAMINOAZOBENZENE
 LYSOSOMAL ENZYME ACTIVITY, RAT LIVER
 LYSOSOMES (1784)
 MITOTIC RATES, LIVER CELL PARENCHYMA
 (1782)
 METHYLBENZANTHRACENE
 ESTROUS CYCLE, RESERPINE, MAMMARY
 GLAND CARCINOMA, RAT (1794)
 12-DIMETHYLBENZ(A)ANTHRACENE
 MAMMARY ADENOCARCINOMA, DISTAL SMALL
 BOWEL BYPASS (1792)
 MAMMARY GLAND CELL NUCLEI, RNA
 POLYMERASE ACTIVITY, RAT (1791)
 MAMMARY GLAND TUMOR, ANTISERA, RAT
 (1990)
 METABOLISM, OVARIAN TUMORS, MICE
 (1787)
 METHYLTHIOURACIL, L-THYROXINE, RAT
 (1790)
 SIMIAN ADENOVIRUS 7, TUMOR TRANSPLANT
 IMMUNITY (1982)
 THYMIC LYMPHOMA, LEUKEMOGENIC
 ACTIVITY (1896)
 TOOTH SOCKET, MANDIBULAR LYMPHOMA
 (1788)
 TUMOR, SKIN, LUNG, MOUSE FETUS (1797)
 URETHAN, GAMMA-IRRADIATION, HORMONE
 (1789)
 URETHAN, IMMUNE RESPONSE IN RATS
 (1989)
 METHYLNITROSAMINE
 HISTOLOGY OF TUMORS, KIDNEY TUMORS,
 RAT (1810)

RENAL ADENOCARCINOMAS, ULTRASTRUCTURE
 (1809)
 RENAL MESENCHYMAL TUMORS, PROGRESSION
 OF NEOPLASTIC CHANGE (1808)
 ULTRASTRUCTURE, RENAL MESENCHYMAL
 TUMOR, RAT (1807)
 DISEASE
 AMEBIC GRANULOMA, CECUM, ADENO-
 CARCINOMA (2123)
 DIABETES MELLITUS, CANCER INCIDENCE
 AND MORTALITY, PANCREATIC CANCER
 (1724)
 PARASITISM, CARCINOGENESIS,
 BILHARZIOSIS, TOXOPLASMOSIS (1727)
 DNA
 N-ACETOXY-2-ACETYLAMINOFLUORENE,
 BINDING (1772)
 N-ACETOXY-2-ACETYLAMINOFLUORENE,
 POLYNUCLEOTIDES (1774)
 EPSTEIN-BARR VIRUS, METAPHASE CHROMO-
 SOMES (1881)
 B-GLUCURONIDASE, BLADDER TUMORS, HUMAN
 (2084)
 METHYLATION, TUMOR CHROMATIN (2100)
 3-METHYLCHOLANTHRENE, MAMMARY TUMORS,
 MURINE (1802)
 4-NITROQUINOLINE-1-OXIDE, INTERACTION,
 MODEL (1825)
 POLYMERASE, BIRD, VIRUS (1943)
 POLYMERASE, CHRONIC LYMPHOCYTIC
 LEUKEMIA, PLASMA (2082)
 POLYMERASE, INFECTED CHICK CELLS,
 MYELOCYTOMATOSIS VIRUS (1893)
 POLYMERASE, ROUS SARCOMA VIRUS,
 SYNTHESIS KINETICS (1941)
 RNA, CHINESE HAMSTER, SV40 (1954)
 SHOPE FIBROMA VIRUS, RK13, LACK OF
 HOMOLOGY (1949)
 SV40, SUPERHELICAL, NICKED (1951)
 SYNTHESIS, LEUKOCYTE, EPSTEIN-BARR
 VIRUS (1884)
 SYNTHESIS, MOUSE EPIDERMIS, HYDRO-
 CORTISONE, CHALONE, CROTON OIL
 (2059)
 SYNTHESIS, NEOPLASTIC CELLS,
 PHYTOHEMAGGLUTININ (1997)
 SYNTHESIS, SV40, 3T3 (1952)
 EAR
 CARCINOMA, 3,3'-DICHLORO-4,4'-DIAMINO-
 DIPHENYL-ETHER, RAT (1767)
 ENDOMETRIUM
 CARCINOMA, FALLOPIAN TUBE HYPERPLASIA,
 HUMAN (2027)
 ENVIRONMENT
 CARCINOGENS, INDUSTRY, ANIMAL FOOD,
 AIR AND WATER (1747)
 HUMAN MALIGNANCY, CHROMOSOMES, HAZARDS
 (2101)
 ENZYME
 ACID AND ALKALINE NUCLEASE, BRAIN,
 MALIGNANCIES (2080)
 ACTIVITIES, RAUSCHER LEUKEMIA VIRUS
 (1907)
 BENZO(A)PYRENE HYDROXYLASE,
 3-METHYLCHOLANTHRENE, PUROMYCIN,
 MICROSOMES (1805)

- BENZO(A)PYRENE HYDROXYLASE, TOBACCO, PLACENTA (1799)
CATALASE, LIVER TUMOR, ETHYL-ALPHA-P-CHLOROPHOXYISOBUTYRATE (2114)
DNA POLYMERASE, CHRONIC LYMPHOCYTIC LEUKEMIA, PLASMA (2082)
DNA POLYMERASE, MYELOCYTOMATOSIS VIRUS, CHICK CELLS (1893)
DNA POLYMERASE, VIRUS, MC29 TUMOR (1892)
GLUCOSE-6-PHOSPHATASE, HORMONE, LIVER, DIETHYLNITROSAMINE (1814)
B-GLUCURONIDASE, DNA, BLADDER TUMORS, HUMAN (2084)
B-GLUCURONIDASE, PHENOLPHTHALEIN, CARCINOMA, MELANOMA, MOUSE (2085)
GLYCOGEN SYNTHETASE, GLYCOGEN, HEPATOMAS, RAT (2086)
GLYCOSYLTRANSFERASE ACTIVITY, POLYOMA, BHK (1958)
HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE, ADENINEPHOSPHORIBOSYLTRANSFERASE, LEUKOCYTES (2083)
LIVER ARGINASE, EHRLICH ASCITES TUMOR, UREA CYCLE ENZYMES (2067)
LYSOSOMAL ACTIVITY, 4-DIMETHYLAMINO-AZOBENZENE, RAT LIVER LYSOSOMES (1784)
METHYLASE, CHROMATIN, HISTONE (2097)
METHYLASE, DNA, TUMOR CELL CHROMATIN (2100)
NUCLEOSIDE DEAMINASE ACTIVITY, SPLEEN, FRIEND LEUKEMIA VIRUS, MOUSE (1901)
RNA POLYMERASE ACTIVITY, 7,12-DIMETHYLBENZ(A)ANTHRACENE, MAMMARY GLAND CELL NUCLEI, RAT (1791)
TRANSFER RNA METHYLASE, NEOPLASTIC HAMSTER TISSUES (2088)
TRANSFER RNA METHYLASE, VIRUS-TRANSFORMED CELLS (1950)
TRANSFER RNA METHYLASE ACTIVITY, CHRONIC LYMPHOCYTIC LEUKEMIA, PHYTOHEMAGGLUTININ (2091)
TYROSINE AMINOTRANSFERASE, 5-BROMODEOXYURIDINE, RAT HEPATOMA CELLS (2078)
TYROSINE HYDROXYLASE ACTIVITY, INHIBITION, HUMAN NEUROBLASTOMA (2064)
- EPIDEMIOLOGY
CANCER, CHILDREN, ITALY (2055)*
CANCER INCIDENCE IN AFRICA, ETIOLOGICAL ASSOCIATIONS (2040)
CANCER MORTALITY, INCIDENCE, GERMANY (2053)*
CERVICAL ATYPIA, COMPUTERIZED STUDY (2045)
CERVICAL CANCER, RISK IN PAROUS INDIAN WOMEN (2042)
CHILE, RAINFALL, ESOPHAGEAL CANCER INCIDENCE (2037)
GENETIC AND ENVIRONMENTAL CLUSTERS, HUMAN AND BOVINE LYMPHOSARCOMA, FAMILIAL CLUSTERS (2096)
INDIA, CANCER INCIDENCE, BUCCO-PHARYNGEAL, CERVICAL (2038)
KOREA, MALIGNANT NEOPLASMS (2054)*
LUNG CANCER, TOBACCO (1741)
LUNG CANCER MORTALITY, AIR POLLUTION, AUSTRALIAN IMMIGRANTS (2049)
LYMPHOSARCOMA, LEUKEMIA, DOGS (2039)
SOUTHERN IRAN, SKIN CANCER INCIDENCE (2041)
TUMOR, AGE, REVIEW (1725)
- EPIDERMIS
EPIDERMIZATION, 3-METHYLCHOLANTHRENE, UTERUS, MICE (1804)
HYDROCORTISONE, CHALONE, DNA SYNTHESIS, MOUSE (2059)
MALIGNANT FIBROBLASTS, DIFFERENTIATION FACTOR (2075)
ULTRASTRUCTURAL STUDY, SUNLIGHT EXPOSURE, HUMAN (1855)
- ESOPHAGUS
CANCER INCIDENCE, CHILE, RAINFALL (2037)
- ESTROGEN
CARCINOMA, RNA AND DNA METABOLISM (1770)
DIETHYLSTILBERTROL, ESTRADIOL, CHANGE IN CERVICAL EPITHELIUM, MONKEYS (1769)
GROWTH OF TUMOR, ESTROGEN-DEPENDENT MAMMARY TUMOR (1993)
- ETHYL METHANESULFONATE
URETHAN, MEIOTIC ABNORMALITIES (1828)
- FALLOPIAN TUBE
HYPERPLASIA, ENDOMETRIAL CARCINOMA, HUMAN (2027)
- FIBROMA
GERBIL CELL LINE, INTRACISTERNAL TYPE A PARTICLES (1869)
- FIBROSARCOMA
INDUCTION, X-IRRADIATION, HUMAN (1849)
- 2-FLUORENYLACETAMIDE
TRNA, BINDING, RAT LIVER (1773)
- FREUND ADJUVANT
TUMOR TRANSPLANTATION, METASTASES, RAT (2022)*
- GENETICS
ADMIXTURE, CANCER, NEGRO (2094)
FAMILIAL LEUKEMIA, HUMAN AND BOVINE LYMPHOSARCOMA, CLUSTERS (2096)
PREDISPOSITION, CELTIC POPULATION, MALIGNANT MELANOMA (2093)
- GLIOBLASTOMA
ASTROCYTOMA, N-NITROSOMETHYLUREA, RAT (1991)
- GLIOMA
ASTROCYTOMAS, N-NITROSAOMETHYLUREA, RAT (1821)
HETEROLOGOUS ANTIGLIOMA "CARRIER" ANTIBODIES, HUMAN (2018)
- GLYCOGEN
GRANULES, HUMAN MENINGOTHELIAL MENINGIOMAS (2104)
- GLYCOPROTEIN
CANDIDA ALBICANS, 3-METHYLCHOLANTHRENE COCARCINOGEN, RODENT (1801)
- GROWTH
ALTERATION OF VIRUS IN CULTURE,

MURINE SARCOMA, FELINE LEUKEMIA (1934)
 CHICK EMBRYO, EHRLICH ASCITES CARCINOMA, METASTASES (2144)*
 CONTROL, PHOSPHATE, URIDINE, TRANSPORT INHIBITORS, 3T3 (1960)
 ENHANCEMENT, 3-METHYLCHOLANTHRENE, MURINE SARCOMA (1986)
 FELINE LEUKEMIA VIRUS, IN HUMAN CELLS (1895)
 HERPES SIMPLEX VIRUS, BURKITT'S LYMPHOMA CELLS (1923)
 INHIBITORS, LIVER, HEPATOMA, ARGINASE, RAT (2072)
 KINETICS, TRANSFORMED CELLS, DEATH RATE (2052)
 MALIGNANT FIBROBLASTS, EPIDERMIS, DIFFUSIBLE FACTOR, DIFFERENTIATION (2075)
 PHASE, VIRUS-TRANSFORMED CELLS, SURFACE GLYCOPROTEINS (1939)
 RATE, CANCER CELLS, METASTASES, PROLIFERATION, GOMPERTZIAN CURVE (1732)
 REPLICATION OF VIRUS, FRIEND VIRUS, BACTERIAL ANTIGENS (1899)
 TUMOR, PATHOGENESIS, SARCOMA (1729)
 HAPTEN
 IMMUNOGLOBULIN A, MYELOMA (2008)
 ERYTHROPOIESIS
 SPLEEN, FRIEND LEUKEMIA VIRUS, RADIATION (1898)
 TESTOSTERONE, RADIATION (1848)
 HEMOGLOBIN
 LEUKEMIA CELL, MURINE VIRUS (1897)
 HEPATOMA
 MORRIS, PROLIFERATION KINETICS (2050)
 MORRIS, TRANSFER RNA, ALTERATIONS (2090)
 HISTOCHEMISTRY
 MUCOSUBSTANCE, CERVICAL CARCINOMA (2109)
 HISTOGENESIS
 AMYLOID STROMA, THYROID, MEDULLARY CARCINOMA, ELECTRON MICROSCOPY (2111)
 ODGKIN'S DISEASE
 LYMPHOMA, THYMOMA, CONNECTIVE TISSUE ULTRASTRUCTURE (2113)
 TONSILLECTOMY (2019)
 HORMONE
 ACTH SYNDROME, OAT CELL CARCINOMA (2103)
 ANDROGEN SECRETION, ENDOCRINE IMBALANCE, MAMMARY CARCINOMA (1751)*
 ANTIGENICITY, CARCINOMA (1740)
 DEPENDENT, MURINE MAMMARY TUMORS (2112)
 ESTROUS CYCLE, DIMETHYLBENZANTHRACENE, MAMMARY GLAND CARCINOMA, RAT (1794)
 GLUCOCORTICOID, INSULIN, GLUCOSE-6-PHOSPHATASE, DIETHYLNITROSAMINE (1814)
 HYDROCORTISONE
 CHALONE, DNA SYNTHESIS, MOUSE EPIDERMIS (2059)

4-HYDROXYAMINOQUINOLINE-1-OXIDE
 DERIVATIVES OF CARCINOGEN,
 CARCINOGENICITY IN MICE AND RATS (1827)
 N-HYDROXY-3-FLUORENYLACETAMIDE
 FLUORENYLACETAMIDE, TRNA, BINDING, RAT LIVER (1773)
 7-HYDROXYTHEOPHYLLINE
 MICE, AMYLOIDOSIS, RETICULOSARCOMA, LUNG ADENOMA (1764)
 IMMUNITY
 ANTIGENS, RHABDOMYOSARCOMA, MOUSE (1987)
 ANTITUMOR REACTIONS, TUMOR ANTIGENS (1754)*
 AVIAN LEUKOSIS, VIRAL ANTIGEN, CHICKEN (1964)
 CANCER, VIRUS, RATS, MICE, REVIEW (1734)
 EHRLICH ASCITES TUMOR, SPLEEN CELLS, MICE (1999)
 FRIEND DISEASE VIRUS, MYCOBACTERIUM BOVIS (1903)
 IMMUNE DEFICIENCY, PREDISPOSITION, LYMPHOID MALIGNANCIES (1723)
 IMMUNIZATION, LEUKEMIA, RADIATION VIRUS (1968)
 ISOGRAFTS, SARCOMA, RNA MURINE (1988)
 LYMPHOCYTES, NEPHROBLASTOMA, HUMAN (2015)
 PARASITE, TUMOR GROWTH, NEMATODE INFECTION (2118)
 SARCOMAS, CELL-SURFACE ANTIGEN, HUMAN (2016)
 SEROLOGIC SPECIFICITY, FREUND ADJUVANT TRNA, METHYLATION (2089)
 SERUM IMMUNOGLOBULINS, CHRONIC LYMPHOCYTIC LEUKEMIA (2011)
 TRANSFER, IMPAIRMENT, GUINEA PIG HEPATOMA (1992)
 TUMOR, HAMSTER, SV40 (1979)
 TUMOR TRANSPLANT, 7,12-DIMETHYLBENZ-(A)ANTHRACENE, SIMIAN ADENOVIRUS 7 (1982)
 IMMUNOCYTOMA
 IMMUNOGLOBULIN, REVIEW (1737)
 IMMUNOGLOBULIN
 A, HAPTEN, MYELOMA (2008)
 A, MYELOMA, HUMAN (2007)
 ANTIGEN-BINDING, MYELOMA PROTEINS, M-COMPONENTS (1736)
 IMMUNOCYTOMA, REVIEW (1737)
 LYMPHOMA, GOLGI COMPLEX, ENDOPLASMIC RETICULUM (2009)
 MYELOMA, IG62B, MOUSE (2005)
 SPLEEN AND LYMPH NODE IGM, BOVINE LEUKOSIS (2013)
 IMMUNOLOGY
 ESTROGEN DEPENDENT MAMMARY TUMOR, IMMUNIZATION, GROWTH (1993)
 HEMADSORPTION REACTION, LEUKEMIA, FELINE, HUMAN (1976)
 MYELOMA PROTEINS, MEDULLARY AND EXTRAMEDULLARY PLASMACYTOMA (2020)*
 SEROLOGICAL STUDY, CHILDHOOD NEOPLASMS (2021)*

- TONSILLECTOMY, HODGKIN'S DISEASE (2019)
TUMOR SPECIFIC, TRANSPLANTATION, ANTIGEN, GLYCOPROTEINS, REVIEW (1758)*
- IMMUNOSUPPRESSION
AZATHIOPRINE, CHROMOSOMAL MUTATIONS, HUMAN LEUKOCYTES, METAPHASES (1766)
LIVER, DIETHYLNITROSAMINE, RAT (1815)
TRANSPLANTATION OF TUMORS, BOVINE LYMPHOSARCOMA (2012)
URETHAN, 7,12-DIMETHYLBENZ(A)ANTHRACENE, RAT (1989)
- INFECTIVITY
SV40, DNA, SUPERHELICAL, NICKED (1951)
- INHIBITOR
5-BROMODEOXYURIDINE, RAT HEPATOMA CELLS, TYROSINE AMINOTRANSFERASE (2078)
DNA IODODEOXYPYRIDINE, CYTOSINE ARABINOSIDE, BURKITT'S LYMPHOMA (1971)
TRANSPORT, GROWTH URIDINE, PHOSPHATE, 3T3 (1960)
- INTERFERON
POLY I.C, HERPESVIRUS SAIMIRI (1918)
- INTESTINE
CARCINOMA, SULFATED MUCOSUBSTANCES, COLONIC AND RECTAL (2066)
CECUM, AMEBIC GRANULOMA, ADENOCARCINOMA (2123)
COLONIC MUCOSA, CARCINOMA, 35 SULFUR UPTAKE (2069)
DISTAL SMALL BOWEL BYPASS, 7,12-DIMETHYLBENZ(A)ANTHRACENE, MAMMARY ADENOCARCINOMA (1792)
INTRAUTERINE CONTRACEPTIVE DEVICE HORMONAL, CANCER, ANIMALS (1742)
- IODINE
PHAGOCYTOSIS, LEUKEMIA, HUMAN (2063)
- KARYOTYPE
RING CHROMOSOME, BENIGN HUMAN MENINGIOMA (2092)
- KIDNEY
DIMETHYLNITROSAMINE, HISTOLOGY OF TUMORS, RAT (1810)
GIANT RENAL CYST, ADENOCARCINOMA, IRRADIATION (1861)*
MOLONEY MURINE SARCOMA VIRUS, TRANSFORMATION IN VITRO (1937)
NEPHROBLASTOMA, LYMPHOCYTES, IMMUNOLOGIC REACTION, HUMAN (2015)
RENAL ADENOCARCINOMAS, ULTRASTRUCTURE, DIMETHYLNITROSAMINE (1809)
RENAL MESENCHYMAL TUMOR, DIMETHYLNITROSAMINE, ULTRASTRUCTURE, RAT (1807)
RENAL MESENCHYMAL TUMORS, PROGRESSION OF NEOPLASTIC CHANGES, DIMETHYLNITROSAMINE (1808)
RENAL TUMORS, HEPATECTOMY, DIETHYLNITROSAMINE, RAT (1812)
- LARYNX
NORMAL AND NEOPLASTIC TISSUES, CELL PROLIFERATION KINETICS, HUMAN (2051)
- LEUKEMIA
ACUTE, CHRONIC MYELOGENOUS, CHRONIC LYMPHATIC, HAPTOGLOBIN (2010)
ADENOVIRUS, STRONTIUM 90, SWINE (1838)
AUTOCHTHONOUS LYMPHOCYTE STIMULATION (1995)
BACTERIA, TUMORS (2124)
CHLOROLEUKEMIA, GRANULOCYTIC, KARYOTYPE STUDIES, RAT (1803)
CHROMOSOMAL ANOMALIES, DOWN'S SYNDROME, BLOOM'S SYNDROME, REVIEW (1756)*
CHRONIC LYMPHOCYTIC, PHYTO-HEMAGGLUTININ, RNA METHYLASE ACTIVITY (2091)
CHRONIC LYMPHOCYTIC, PLASMA, DNA POLYMERASE (2082)
CHRONIC LYMPHOCYTIC, SERUM IMMUNOGLOBULINS (2011)
CHRONIC MYELOCYTIC, PHILADELPHIA CHROMOSOME (1730)
CHRONIC MYELOGENOUS, STORAGE CELL ULTRASTRUCTURE, GAUCHER'S DISEASE (2110)
COW LYMPHOCYTES, BOVINE LYMPHOCYTOSIS, C-TYPE VIRUS PARTICLES (1877)
DOG BITE, CHILDHOOD (2133)
FELINE, VIRUS (1894)
FELINE, VIRUS, GROUP-SPECIFIC ANTIGEN (1977)
GROSS VIRUS, BITTNER VIRUS, MAMMARY GLAND TUMOR, MOUSE (1928)
GROSS VIRUS, CHROMOSOMES, MICE (1904)
GROSS VIRUS, IMMUNOLOGY, GENETICS (1970)
HAPTOGLOBIN TYPES (2023)*
HEMADSORPTION REACTION, FELINE, HUMAN (1976)
HERPES-LIKE VIRUS, GUINEA PIG (1920)
HUMAN LEUKEMIC CELLS, EPSTEIN-BARR VIRUS (1882)
HUMAN LYMPHOID, BLOOD LYMPHOCYTE CELL MEMBRANE, ULTRASTRUCTURE OF ACID CARBOHYDRATES (2142)*
HUMAN PERIPHERAL BLOOD, HERPES TYPE VIRUS (1925)
HYDROGEN TRANSPORT, BONE MARROW, HUMAN (2060)
IMMUNE LYMPHOCYTES, VIRUS ANTIGEN, SUPPRESSION OF TUMOR GROWTH (1969)
INCIDENCE AMONG DOGS, LYMPHOSARCOMA (2039)
INDUCTION, HUMAN LEUKEMIC CELLS, MONKEYS (1867)
INDUCTION, STRONTIUM 90, X-IRRADIATION (1839)
INDUCTION IN MICE, HUMAN LYMPHOMA CELLS, LATENCY (2136)
LEUKEMOGENIC VIRUS, GUINEA PIG (1871)
MAMMARY TUMORS, C-TYPE VIRUS PARTICLES, RAT (1870)
MAST CELL, TRANSPLANTATION OF TUMOR, CANINE (2131)
MOLONEY VIRUS, TRANSMISSION, CHROMOSOME (1905)
MONOCYTIC, MYELO-MONOCYTIC, ULTRASTRUCTURE, HUMAN (2115)
MOUSE LEUKEMIA VIRUS, IMMUNOTHERAPY, ETIOLOGY, MONONUCLEOSIS (1738)

MURINE, POLYAMINE ACCUMULATION,
 SPERMIDINE AND PUTRESCINE SYNTHESIS
 (2074)
 MYCOTOXINS, TUMOR, MICE (1776)
 PHAGOCYTOSIS, IODINE, HUMAN (2063)
 PHILADELPHIA CHROMOSOME (1753)*
 RADIATION, BONE MARROW AUTOTRANSPLANT,
 MOUSE (1864)*
 RADIATION VIRUS, IMMUNIZATION (1968)
 RAUSCHER LEUKEMIA VIRUS, CHANGES IN
 ENZYME ACTIVITY (1907)
 STRONTIUM 90, MYELOID NEOPLASMS IN
 SWINE (1841)
 STRONTIUM 90, X-IRRADIATION (1839)
 TUMOR ISOLATES, MYCOBACTERIA (2125)
 VIRAL, MYELOID, STAPHYLOCOCCUS,
 CHICK (1889)
 VIRUS, GROUPS SPECIFIC ANTIGEN, FELINE
 (1975)
 VIRUS PARTICLES IN GUINEA PIG,
 TRANSMISSION (1865)
 KOCYTE
 ADENINE PHOSPHORIBOSYLTRANSFERASE,
 HYPOXANTHINE PHOSPHORIBOSYLTRANS-
 FERASE (2083)
 HUMAN PERIPHERAL BLOOD, LEUKEMIA,
 HERPES TYPE VIRUS (1925)
 LITHIUM TREATMENT, MANIC DEPRESSIVE
 SYNDROME (1835)
 KOPLAKIA
 URETRAL CALCULUS (2141)*
 KOSIS
 AVIAN, COMPLEMENT FIXING ANTIGEN,
 ROUS SARCOMA VIRUS (1966)
 BOVINE, SWEDEN, LYMPHOCYTOSIS (2130)
 COINCIDENCE IN CATTLE HERDS, BOVINE
 LYMPHOCYTOSIS (2128)
 COMPARISON, BOVINE LEUKOTIC VIRUS-LIKE
 PARTICLES, FELINE LEUKOSIS VIRUS
 (1874)
 HUMAN AND BOVINE, INCIDENCE IN
 BALTIMORE U.S.S.R. (2048)
 IMMUNOGLOBULIN, SPLEEN AND LYMPH NODE
 IGM, BOVINE (2013)
 RNA, AVIAN VIRUS (1887)
 ONENE
 DIBENZOPYRENE, TRICAPRYLIN, ADENOMA,
 MOUSE (1795)
 ID
 LIVER, NEOPLASMS, HUMAN (2058)
 PROTEOLIPID, WALKER RAT SARCOMA,
 ISOLATION (2068)
 OGRANULOMA
 HUMAN LIVER BIOPSY, FATTY CHANGE IN
 LIVER (2102)
 SCLEROSING, PARAFFINOMA, MINERAL OIL
 INJECTIONS (1860)
 OMA
 CHLORPROPAMIDE (1830)
 OSARCOMA
 METHYLCHOLANTHRENE, IMMUNOTHERAPY,
 GUINEA PIG (1984)
 HUM
 MANIC DEPRESSIVE SYNDROME, BLOOD
 LEUKOCYTES (1835)
 ER
 N-ACETYLATION, HEPATOMA HISTONE, RAT
 (2056)
 AFLATOXIN, CYTOPLASM, ENDOPLASMIC
 RETICULUM, MITOCHONDRIA, RATS (1780)
 AFLATOXIN, SUBACUTE CHANGES, BEAGLE
 (1778)
 CANCER, BANTU, CARCINOGENIC MYCOTOXIN
 (2135)
 CARCINOMA, AFLATOXIN CONSUMPTION,
 SWAZILAND (1781)
 CARCINOMA, ALPHA-FETOPROTEIN (2003)
 CARCINOMA, 4-NITROQUINOLINE-1-OXIDE,
 TRANSPLANTABLE TUMOR LINE, RAT
 (1824)
 CELL NUCLEI RNA POLYMERASE,
 N,N-DIMETHYL-4-AMINOAZOBENZENE, RAT
 (1783)
 CELL REGENERATION, MITOTIC RATES,
 4-DIMETHYLAMINOAZOBENZENE (1782)
 DIETHYLNITROSAMINE, PARTIAL HEPA-
 TECTOMY, RENAL TUMORS (1812)
 FATTY CHANGE, LIPOGRANULOMA, HUMAN
 (2102)
 GLUCOSE-6-PHOSPHATASE, HORMONE,
 DIETHYLNITROSAMINE (1814)
 GLYCOGENOSIS, HEPATOMAS, ULTRASTRUCTURE,
 HUMAN (2073)
 HEPATOCELLULAR CHANGES, GLYCOGEN,
 N-NITROSOMORPHOLINE (1818)
 HEPATOMA, AZO DYE, ULTRASTRUCTURE,
 RAT (1785)
 HEPATOMA, TUMOR IMMUNITY, GUINEA PIG
 (1992)
 IMMUNOSUPPRESSORS, RATS, DIETHYL-
 NITROSAMINE (1815)
 LIPIDS, NEOPLASMS, HUMAN (2058)
 LYSOSOMES, 4-DIMETHYLAMINOAZOBENZENE,
 LYSOSOMAL ACTIVITY, RAT (1784)
 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE,
 3-METHYLCHOLANTHRENE, RAT (1786)
 MITOTIC RATES, 4-DIMETHYLAMINO-
 AZOBENZENE, REGENERATION (1782)
 NITROSOHEXAMETHYLENAMINE, ULTRA-
 STRUCTURAL STUDY, RAT (1817)
 NORMAL, HEPATOMA, GROWTH INHIBITOR,
 RAT (2072)
 NOVIKOFF ASCITES HEPATOMA CELLS,
 CYTOPLASMIC GLYCOGEN FOCI, GLUCOSE
 INCORPORATION (2061)
 PRIMARY CANCER, ALPHA-FETOPROTEINS,
 LOCALIZATION, HUMAN (2004)
 PRIMARY CANCER, CIRRHOSIS, GIANT CELL
 HEPATITIS, INFANT (2032)*
 RAT HEPATOMA CELLS, TYROSINE AMINO-
 TRANSFERASE, 5-BROMODEOXYURIDINE
 (2078)
 RNA METABOLISM, THIOACETAMIDE, RAT
 (1775)
 SPLEEN, SCHISTOSOMIASIS, FOLLICULAR
 LYMPHOMA (2122)
 TRNA, MORRIS 5123 HEPATOMA (2025)
 TUMOR, ETHYL-ALPHA-P-CHLOROPHOENOXISO-
 BUTYRATE, LIVER CATALASE, RAT (2114)
 TUMORS, NEWBORN AND ADULT HAMSTERS,
 CYCASIN (1765)
 UREA CYCLE ENZYMES, ARGINASE, EHRlich
 ASCITES TUMOR (2067)
 LUNG
 ADENOMA, BIS(CHLOROMETHYL) ETHER,
 CHRONIC INHALATION, MICE (1761)

- ADENOMA, RETICULOSARCOMA, AMYLOIDOSIS,
7-HYDROXYTHEOPHYLLINE (1764)
ADENOMA, TRANSPLACENTAL EFFECT,
DIETHYLNITROSAMINE, MOUSE (1816)
ALVEOLI, PLUTONIUM AEROSOL, RAT (1843)
BRONCHIAL EPITHELIUM, DRY WEIGHT AND
HYDRATION CHANGES, CO 60-GAMMA
IRRADIATION (1850)
BRONCHOALVEOLAR CARCINOMA, PULMONARY
ADENOMATOUS CHANGE (2139)
CANCER, EPIDEMIOLOGY, TOBACCO (1741)
CANCER, FINLAND, TUBERCULOSIS (2117)
CANCER CELLS, LYMPHOCYTE INTERACTIONS,
HUMAN (2079)
CANCER MORTALITY, NASAL CANCER, NICKEL
PLANT WORKERS (2043)
CARCINOMA, INDUSTRIAL CARCINOGENS,
PRIMATES, RODENTS, REVIEW (1747)
CARCINOMA, TISSUE TYPE, URANIUM MINERS
(1859)
GRANULOMAS, ASBESTOS DUST, MICE,
HAMSTERS (1852)
HYPERPLASIA, FOCAL PROLIFERATION,
TOBACCO, RABBIT (1833)
MESOTHELIOMA, ASBESTOS EXPOSURE,
ENGLAND (1858)
PULMONARY ADENOMATA, 3-METHYL-
CHOLANTHRENE, MICE (1806)
PULMONARY FIBROSARCOMA, DIABETES
MELLITUS (2145)*
PULMONARY FUNCTION, ASBESTOS DUST,
OCCUPATIONAL EXPOSURE (1857)
TOBACCO, EMPHYSEMA, SPONTANEOUS
PNEUMOTHORAX, CANCER (1834)
TUMORS, INDUSTRIAL CARCINOGENS, REVIEW
(1749)
TUMORS, INDUSTRIAL CARCINOGENS, TUMOR
MORPHOLOGY (1750)
TUMORS, POLYVINYLPYRIDINE-N-OXIDE,
INHALATION (1768)
LYMPHOBLAST
CYTOGENETICS, EPSTEIN-BARR VIRUS
(1884)
LYMPHOCYTE
INTERACTIONS, HUMAN LUNG CANCER CELLS
(2079)
MIXED REACTION, AUTOCHTHONOUS STIMULA-
TION, LEUKEMIA (1996)
THYMIC, X-IRRADIATION, NUCLEOLAR
MORPHOLOGY (1842)
TRANSFORMATION, PHYTOHEMAGGLUTININ,
CANCER PATIENTS (1998)
LYMPHOCYTOSIS
BOVINE LEUKOSIS, COINCIDENCE IN CATTLE
HERDS (2128)
LYMPHOMA
ENDOPLASMIC RETICULUM, GOLGI COMPLEX,
IMMUNOGLOBULIN (2009)
HAMSTER PAPILLOMAS, PAPOVA VIRUS
(1956)
HUMAN CELLS, INDUCTION OF LEUKEMIA IN
MICE, LATENCY (2136)
MALIGNANT, HERPESVIRUS SAIMIRI,
MONKEYS (1917)
MANCIBULAR, 7,12-DIMETHYLBENZ(A)-
ANTHRACENE, TOOTH SOCKET (1788)
PHYTOHEMAGGLUTININ, DNA SYNTHESIS,
MURINE (1997)
THYMUS, LEUKEMOGENIC ACTIVITY,
7,12-DIMETHYLBENZ(A)ANTHRACENE
(1896)
LYMPHOPROLIFERATIVE DISEASE
LYMPHOID MALIGNANCIES, IMMUNE
DEFICIENCY, PREDISPOSITION (1723)
PATHOGENESIS, IMMUNOLOGICAL DISORDERS
REVIEW (1760)*
LYMPHOSARCOMA
BOVINE, VIRUS IN BOVINE CELLS (1873)
CYTOPATHIC EFFECT, MIXED CELL
CULTURES, VIRUS, BOVINE (1876)
LYMPHOCYTES, SPLEEN, BOVINE (2036)
THYMUS, PIKE (2126)
TRANSMISSION OF DISEASE, FELINE,
EPIDEMIOLOGY (2044)
TRANSMISSION OF DISEASE, VIRUS
PARTICLES, BOVINE (2129)
TRANSPLANTATION OF TUMORS, IMMUNO-
SUPPRESSION, BOVINE (2012)
TRANSPLANTATION PASSAGE IN DOGS,
GUINEA PIG, CANINE (2132)
MAMMARY GLAND
ADENOCARCINOMA, DISTAL SMALL BOWEL
BYPASS, 7,12-DIMETHYLBENZ(A)ANTHRA-
CENE (1792)
BENIGN, MALIGNANT, FIBROSA CYSTICA,
FIBROMATOSIS, FIBROADENOMA (2029)
BITTNER VIRUS, LEUKEMIA, GROSS VIRUS,
MOUSE (1928)
BREAST CANCER MORTALITY, REGIONAL
VARIATIONS IN ENGLAND, DAIRY PRODUCT
CONSUMPTION (2047)
CANCER, ANTIBODIES, MURINE MAMMARY
TUMOR VIRUS (1929)
CARCINOMA, ANDROGEN SECRETION, ENDO-
CRINE IMBALANCE (1751)*
CARCINOMA, DIMETHYLBENZ(A)ANTHRACENE,
ESTROUS CYCLE, RAT (1794)
CARCINOMA, ETIOLOGY, PATHOGENESIS,
REVIEW (1757)*
7,12-DIMETHYLBENZ(A)ANTHRACENE,
NUCLEAR RNA POLYMERASE ACTIVITY,
RAT (1791)
MULTIPLE TUMORS, CERVIX, THERAPY,
INCIDENCE (2137)
NEOPLASIA, IRRADIATED GRAFT,
X-IRRADIATION (1847)
NUCLEAR RNA, NEOPLASTIC DEVELOPMENT,
MURINE (2062)
SPONTANEOUS CARCINOMA, RUDIMENTS, RAT
(2127)
TUMOR, ANTISERA, 7,12-DIMETHYLBENZ(A)
ANTHRACENE, RAT (1990)
TUMOR, HORMONE-DEPENDENT, MURINE
(2112)
TUMOR, LEUKEMIA, C-TYPE VIRUS
PARTICLES, RAT (1870)
TUMOR, 3-METHYLCHOLANTHRENE, DNA
(1802)
TUMOR, NUCLEIC ACIDS (2081)
TUMOR VIRUS, CELL FUSION, MURINE
(1926)
TUMOR VIRUS, RNA, ANTIGEN CROSS-

REACTION (1927)
 AREK'S DISEASE
 CHICKEN EMBRYO, AGENT (1915)
 ASTOCYTOMA
 CELLS, CYTOTOXIC REACTION, PHOSPHO-
 LIPID METABOLISM (2057)
 EIOSIS
 ABNORMALITIES, URETHAN, ETHYL
 METHANESULFONATE (1828)
 ELANIN
 KERATINOCYTES, BASAL CELL CARCINOMA
 (2106)
 ELANOMA
 CARCINOMA, 8-GLUCURONIDASE, PHENOL-
 PHTHALEIN, MOUSE (2085)
 MALIGNANT, CELTIC POPULATION, GENETIC
 PREDISPOSITION (2093)
 RNA, HARDING-PASSEY CELLS, LIVER,
 MUSCLE, RAT (2077)
 EMBRANE
 BLOOD LYMPHOCYTE CELL, ULTRASTRUCTURE
 OF ACID CARBOHYDRATES, HUMAN
 LYMPHOID LEUKEMIA (2142)*
 CELL SURFACE GLYCOPROTEINS, VIRUS,
 GROWTH PHASE (1939)
 GLYCOPEPTIDES, VIRUS-TRANSFORMED
 CELLS, POLYOMA (1957)
 INFECTED CELL, MUCOPOLYSACCHARIDE
 LAYER, FUJINAMI ROUS SARCOMA VIRUS
 (1948)
 ENGIOMA
 BENIGN, RING CHROMOSOME, HUMAN (2092)
 MENINGOTHELIAL, GLYCOGEN GRANULES,
 HUMAN (2104)
 ESOTHELIOMA
 ASBESTOS EXPOSURE, NETHERLANDS
 SHIPYARDS (2046)
 PLEURAL, ENGLAND, ASBESTOS EXPOSURE
 (1858)
 ETABOLISM
 N-ACETYLATION, NORMAL AND NEOPLASTIC
 RAT LIVER, HEPATOMA HISTONE (2056)
 ADENINE NUCLEOTIDE, ASCITES TUMOR
 CELLS, MICE (2065)
 GLUCOSE INCORPORATION, NOVIKOFF
 ASCITES HEPATOMA CELLS, CYTOPLASMIC
 GLYCOGEN FOCI (2061)
 GLYCOGEN, GLYCOGEN SYNTHETASE,
 HEPATOMAS, RAT (2086)
 GLYCOGENESIS, HEPATOMA, ULTRASTRUCTURE
 (2073)
 HYDROGEN TRANSPORT, LEUKEMIA, BONE
 MARROW (2060)
 LIPID, SKIN, LIGHT, RADIATION (1856)
 NUCLEIC ACID, PROLIFERATING COLONIC
 CELLS, NEOPLASTIC LESIONS (2076)
 PHOSPHOLIPID, MASTOCYTOMA CELLS,
 CYTOTOXIC REACTION (2057)
 32 PHOSPHORUS INCORPORATION, MAMMARY
 TUMOR TISSUE (2081)
 PROTEOLIPID, WALKER RAT SARCOMA (2068)
 SPERMIDINE AND PUTRESCINE SYNTHESIS,
 POLYAMINE ACCUMULATION, MURINE
 LEUKEMIA L1210 (2074)
 35 SULFUR UPTAKE, COLONIC MUCOSA,
 CARCINOMA (2069)

METAL
 HUMAN TISSUES, BENIGN, MALIGNANT,
 MICROPROBE ANALYSIS (2134)
 METASTASIS
 EHRlich ASCITES CARCINOMA, GROWTH IN
 CHICK EMBRYO (2144)*
 MALIGNANT TROPHOBLASTIC TERATOMA,
 TESTICULAR TUMORS (2116)
 MURINE PLASMACYTOMA, BONE LESIONS
 (2143)*
 METHYLATION
 GUANOSINE, CYTOSINE, IMMUNITY, TRNA
 (2089)
 NEOPLASTIC HAMSTER TISSUES, TRANSFER
 RNA METHYLASE (2088)
 RNA, DNA, 1-PHENYL-3,3-DIMETHYL-
 TRIAZENE (1762)
 METHYLCHOLANTHRENE
 LIPOSARCOMA, IMMUNOTHERAPY, GUINEA
 PIG (1984)
 SARCOMA, TRANSPLANTATION ANTIGENS,
 GUINEA PIG (1985)
 3-METHYLCHOLANTHRENE
 BENZO(A)PYRENE HYDROXYLASE, PUROMYCIN,
 MICROSOMES (1805)
 COCARCINOGEN, CANDIDA ALBICANS GLYCO-
 PROTEIN, RODENT (1801)
 DNA, MAMMARY TUMORS, MURINE (1802)
 ENHANCEMENT OF TUMOR GROWTH, MURINE
 SARCOMA (1986)
 EPIDERMIZATION, UTERUS, MICE (1804)
 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE,
 LIVER, RAT (1786)
 PULMONARY ADENOMATA, MICE (1806)
 SARCOMA, TRANSFER OF TUMOR RESISTANCE,
 RAT (1983)
 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE
 3-METHYLCHOLANTHRENE, LIVER, RAT
 (1786)
 METHYLNITROSOUREA
 BLOOD BRAIN BARRIER, PERMEABILITY,
 CNS TUMORS, RAT (1822)
 METHYLNITROSOURETHAN, RAT GASTRIC
 TUMORS (1823)
 N-METHYL-N-NITROSOUREA
 FORMATION OF CARCINOGEN IN RAT
 STOMACH, N-METHYLUREA (1820)
 METHYLTHIOURACIL
 L-THYROXINE, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, RAT (1790)
 MICROORGANISM
 URINE, CRYPTOCIDES, TUMOR ISOLATES
 (2120)
 MALIGNANCY, CANCER ISOLATE (2119)
 NEOPLASMS, ISOLATES (2121)
 MICROsome
 BENZO(A)PYRENE HYDROXYLASE, 3-METHYL-
 CHOLANTHRENE, PUROMYCIN (1805)
 MILK
 DNA POLYMERASE, RNA, HUMAN (1878)
 LACTATING HAMSTERS, TUMOR INDUCTION
 IN OFFSPRING, DIETHYLNITROSAMINE
 (1813)
 MINERAL OIL
 PARAFFINOMA, SCLEROSING LIPOGRANULOMA
 (1860)

MITOCHONDRIA
TUMOR, RESPIRATORY IMPAIRMENT, ULTRA-
STRUCTURE, ALTERATION (1731)

MITOSIS
ABERRATIONS, RAT BONE MARROW,
X-IRRADIATION (1844)
RNA, DNA, CHROMOSOMES, REVERSION
(2072)

MORPHOLOGY
PULMONARY ADENOMATOUS CHANGE,
BRONCHOALVEOLAR CARCINOMA (2139)

MUCOSUBSTANCE
SULFATED, COLONIC AND RECTAL MUCO-
SUBSTANCES, CARCINOMA (2066)

MYCOBACTERIA
LEUKEMIA, TUMOR ISOLATES (2125)

MYCOTOXIN
ANIMALS, CANCER, STRUCTURE (1747)
LEUKEMIA, MICE (1776)
STERIGMATOCYSTIN, CARCINOGENIC, LIVER
CANCER, BANTU (2135)
TERATOGENESIS, CHICK EMBRYO (1779)

MYELOBLASTOSIS
VIRAL RNA, BAI AVIAN LEUKOSIS VIRUS
(1890)
VIRUS, AVIAN, ANTIGEN (1967)

MYELOMA
M-COMPONENTS, ANTIGEN-BINDING IMMUNO-
GLOBULINS (1736)
GAMMA GLOBULIN, IGG 2B, MOUSE (2005)
HAPTEN, IMMUNOGLOBULIN A (2008)
IMMUNOGLOBULIN A, HUMAN (2007)
PLASMACYTOMA, PROTEIN STRUCTURE,
MOUSE (2006)
PROTEIN, MEDULLARY AND EXTRAMEDULLARY
PLASMACYTOMAS, IMMUNOLOGICAL
REACTION (2020)*

NASOPHARYNX
CARCINOMA, BURKITT'S LYMPHOMA, HERPES-
TYPE VIRUS (1922)

NEUROBLASTOMA
TYROSINE HYDROXYLASE ACTIVITY,
INHIBITION, HUMAN (2064)

NICKEL
NASAL CANCER, LUNG CANCER, PLANT
WORKER'S (2043)

4-NITROQUINOLINE-1-OXIDE
4-AZOQUINOLINE-1-OXIDE, ANTIBODY TO
CARCINOGEN (1994)
CARCINOGENICITY, ELECTRONIC STRUCTURE,
REVIEW (1745)
DNA, INTERACTION, MODEL (1825)
IN VIVO CARCINOGENICITY, REVIEW (1746)
RAT LIVER CARCINOMAS, TRANSPLANTABLE
TUMOR LINE (1824)

NITROSAMIDES
GASTRIC CANCER, NITROSOURETHAN,
NITROSUREA (1819)

NITROSOHEXAMETHYLENAMINE
RAT LIVER, ULTRASTRUCTURAL STUDY
(1817)

N-NITROSOMETHYLUREA
ASTROCYTOMA, GLIOBLASTOMA, RAT (1991)
ASTROCYTOMAS, GLIOMAS, RAT (1821)

N-NITROSOMORPHOLINE
HEPATOCELLULAR CHANGES, GLYCOGEN
(1818)

NUCLEIC ACID
DNA, RNA, AFLATOXINS, REVIEW (1744)
DNA, RNA, 1-PHENYL-3,3-DIMETHYL-
TRIAZENE, METHYLATION (1762)
MAMMARY TUMOR TISSUE, 32 PHOSPHORUS
INCORPORATION (2081)
NEOPLASTIC COLONIC CELLS, PROLIFERA-
TION (2076)
RNA, DAN, CHROMOSOMES, MITOSIS (2072)

NUCLEOLUS
MORPHOLOGY, THYMIC LYMPHOCYTES,
X-IRRADIATION (1842)

NUCLEOTIDE
POLY I.C, VIRUS, HERPESVIRUS SAIMIRI,
INTERFERON (1918)

OCCUPATIONAL HAZARD
BENZO(A)PYRENE, COKE OVEN (1800)
NETHERLANDS SHIPYARDS, MESOTHELIOMA,
ASBESTOS EXPOSURE (2046)
NICKEL PLANT WORKERS, NASAL CANCER,
LUNG CANCER (2043)
PULMONARY FUNCTION, ASBESTOS DUST
EXPOSURE (1857)
URANIUM MINERS, LUNG CARCINOMA, TISSUE
TYPE (1859)

ORAL CAVITY
BUCCOPHARYNGEAL CANCER, CERVIX, INDIA,
INCIDENCE (2038)
7,12-DIMETHYLBENZ(A)ANTHRACENE,
MANDIBULAR LYMPHOMA (1788)

ORAL CONTRACEPTIVE
CANCER INCIDENCE (1743)
DEPO-MEDROXYPROGESTERONE ACETATE,
CERVICAL MALIGNANCY (1832)
MAMMARY CANCER, ANIMALS, UTERINE
CERVICAL CANCER (1742)

ORGAN TRANSPLANTATION
BRAIN MESENCHYMAL TUMORS, HUMAN (2138)

OVARY
CYSTADENOCARCINOMA, CERVICAL SQUAMOUS
CELL CARCINOMA, TS ANTIGENS (2000)
IONIZING RADIATION, TUMORIGENESIS,
MOUSE (1845)
TUMORS, 7,12-DIMETHYLBENZ(A)ANTHRACENE
METABOLISM, MICE (1787)

OVUM
SV40, MOLONEY SARCOMA VIRUS (1931)

PANCREAS
CANCER, DIABETES MELLITUS, CANCER
INCIDENCE AND MORTALITY, REVIEW
(1724)
PANCREATIC ISLET CELL ADENOMA, ULTRA-
STRUCTURAL STUDY (2105)

PAPILLOMA
LYMPHOMA, PAPOVA VIRUS, HAMSTER (1956)

PARASITE
CANCER, BILHARZIASIS, BLADDER, NERVOUS
SYSTEM, TOXOPLASMOSIS (1727)
NEMATODE INFECTION, TUMOR GROWTH,
IMMUNITY TO PARASITE (2118)

PAROTID GLAND
TUMOR, EPITHELIAL ORIGIN, HUMANS
(2033)*

PATHOGENESIS
CARCINOMA, MAMMARY GLAND, REVIEW
(1757)*

LYMPHOPROLIFERATIVE DISORDERS, IMMUNE
 DEFICIENCY, REVIEW (1760)*
 OVARIAN TUMOR, RADIATION EXPOSURE,
 MOUSE (1845)
 THYROID CANCER, ADENOMA, GOITER,
 HUMANS (2030)
 TUMOR, PAROTID, EPITHELIAL ORIGIN,
 HUMANS (2033)*
 URINE BLADDER TUMOR, DARK CELLS,
 HUMANS (2028)
 ESTROGENS
 CIGARETTE TOBACCO, TUMOR PROMOTION
 (1793)
 ETS
 CHILDHOOD LEUKEMIA, DOG BITES (2133)
 FELINE FIBROSARCOMA, TUMOR INDUCTION
 IN MAMMALS (1872)
 MACROPHAGES
 IODINE, LEUKEMIA, HUMAN (2063)
 PHENOLPHTHALEIN
 MELANOMA, CARCINOMA, B-GLUCURONIDASE,
 MOUSE (2085)
 PHENYL-3,3-DIMETHYLTRIAZENE
 RNA, DNA, METHYLATION (1762)
 HYTOHEMAGGLUTININ
 LYMPHOCYTE TRANSFORMATION, CANCER
 PATIENTS (1998)
 TRANSFER RNA METHYLASE ACTIVITY,
 CHRONIC LYMPHOCYTIC LEUKEMIA (2091)
 LACENTA
 CHORIOCARCINOMA, KIDNEY (2014)
 PLASMACYTOMA
 PROTEIN STRUCTURE, MYELOMA, MOUSE
 (2006)
 POLYVINYLPIRIDINE-N-OXIDE
 LUNG TUMORS IN RATS, INHALATION OF
 CARCINOGEN (1768)
 RECARCINOGENOUS CONDITION
 MELANOSIS, STADE EPHELIDE (2026)
 PROLIFERATION
 CELL KINETICS, NORMAL AND NEOPLASTIC
 TISSUES, HUMAN LARYNGEAL TISSUES
 (2051)
 CONTACT INHIBITION, CARCINOGENESIS
 (1728)
 GROWTH RATE, CANCER CELLS, METASTASES,
 GOMPERTZIAN CURVE (1732)
 KINETICS, MORRIS HEPATOMA (2050)
 PROTEIN
 ALPHA-FETOPROTEIN, CARBOHYDRATE
 ANALYSIS, PROPERTIES (2002)
 ALPHA-FETOPROTEIN, LIVER, CARCINOMA
 (2003)
 ALPHA-FETOPROTEIN, PRIMARY LIVER
 CANCER, LOCALIZATION, HUMAN (2004)
 HAPTOGLOBIN TYPES, LEUKEMIA PATIENTS
 (2023)*
 HEPATOMA HISTONE, N-ACETYLATION,
 NORMAL AND NEOPLASTIC RAT LIVER
 (2056)
 STRUCTURAL, ADENOVIRUS 2 (1912)
 STRUCTURAL, SV40, KIDNEY (1953)
 STRUCTURE, PLASMACYTOMA, MYELOMA,
 MOUSE (2006)
 SYNTHESIS, ADENOVIRUS 2, METHIONINE
 INITIATION (1911)

RADIATION
 ADENOCARCINOMA, GIANT RENAL CYST
 (1861)*
 FRIEND LEUKEMIA VIRUS, HEMATOPOIESIS
 (1898)
 GAMMA IRRADIATION, 7,12-DIMETHYL-
 BENZ(A)ANTHRACENE, URETHAN, HORMONE
 (1789)
 CO 60-GAMMA IRRADIATION, BRONCHIAL
 EPITHELIUM, DRY WEIGHT AND HYDRATION
 CHANGES (1850)
 HEMATOPOIETIC REGENERATION, TESTO-
 STERONE (1848)
 LEUKEMIA, BONE MARROW AUTOTRANSPLANT,
 MOUSE (1864)*
 PLUTONIUM AEROSOL, RAT LUNG ALVEOLI
 (1843)
 RETROMANDIBULAR DAMAGE, THOROTRASTOMA
 (1862)*
 SKIN, LIGHT, LIPID METABOLISM (1856)
 STRONTIUM 90, ADENOVIRUS (1838)
 STRONTIUM 90, MYELOID NEOPLASMS IN
 SWINE, LEUKEMIA (1841)
 SUNLIGHT EXPOSURE, HUMAN EPIDERMIS,
 ULTRASTRUCTURAL STUDY (1855)
 TUMORIGENESIS, OVARY, MOUSE (1845)
 ULTRAVIOLET, FIBROBLASTS, HAMSTER
 (1851)
 ULTRAVIOLET, T ANTIGEN, SV40, ADENO-
 VIRUS 12 (1978)
 UTERUS, CARCINOGENICITY, RAT (1846)
 X-IRRADIATION, ATOMIC BOMB SURVIVORS
 (1851)
 X-IRRADIATION, FIBROSARCOMA INDUCTION,
 HUMAN (1849)
 X-IRRADIATION, LEUKEMIA INDUCTION,
 STRONTIUM 90 (1839)
 X-IRRADIATION, MAMMARY NEOPLASIA,
 IRRADIATED GRAFT (1847)
 X-IRRADIATION, NUCLEOLAR MORPHOLOGY,
 THYMIC LYMPHOCYTES (1842)
 X-IRRADIATION, RAT BONE MARROW,
 MITOTIC ABERRATIONS (1844)
 X-IRRADIATION, SPONTANEOUS LYMPHOMAS,
 VIRUS PARTICLES, HAMSTER (1868)
 X-IRRADIATION, STRONTIUM 90, LEUKEMIA
 INDUCTION (1839)
 RESISTANCE
 TUMOR, TRANSFER, METHYLCHOLANTHRENE,
 RAT SARCOMA (1983)
 RETICULOSARCOMA
 LYMPHOID, HISTIOCYTIC SARCOMA, HISTIO-
 BLASTIC SARCOMA, ULTRASTRUCTURE
 (2108)
 RHABDOMYOSARCOMA
 ANTIGENS, IMMUNITY, MOUSE (1987)
 RNA
 AVIAN LEUKOSIS, VIRUS (1887)
 HARDING-PASSEY CELLS, MELANOMA,
 MUSCLE, RAT LIVER (2077)
 MESSENGER, SARCOMA 180 ASCITES,
 POLYSOME (2071)
 METABOLISM, THIOACETAMIDE, RAT LIVER
 (1775)
 MILK, DNA POLYMERASE, HUMAN (1878)
 MYELOBLASTOSIS, BAI AVIAN LEUKOSIS
 VIRUS (1890)

- NUCLEAR, AFLATOXIN, HEPATOCYTES, RATS (1780)
 NUCLEAR, MAMMARY CELLS, NEOPLASTIC, MOUSE (2062)
 NUCLEOTIDE COMPOSITION, HYBRIDIZATION, VIRUS (1942)
 RIBOSOMAL TRANSFER, BRAIN TUMORS, HUMAN (2087)
 SARCOMA, ISOGRAFTS, MURINE (1988)
 TRANSFER, LIVER, MORRIS 5123 HEPATOMA (2025)
 TRANSFER, MORRIS HEPATOMAS, ALTERATIONS, RAT (2090)
 TRANSFER, POLYOMA VIRUS, RAT (1962)
 VIRION RNA SYNTHESIS (1940)
 VIRUS, MAMMARY TUMORS (1927)
- SARCOMA
 ROUS VIRUS, DEFECTIVE STRAIN, HELPER, CHICKEN EMBRYO (1947)
 STICKER'S TUMOR, ULTRASTRUCTURE, DOG (2107)
 TUMOR GROWTH, PATHOGENESIS (1729)
- SCHISTOSOMIASIS
 HEPATOSPLENIC, SPLENIC FOLLICULAR LYMPHOMA (2122)
- SKIN
 LIPID METABOLISM, LIGHT, IRRADIATION (1856)
 NEUTRAL FRACTION, CIGARETTE SMOKE, BENZO(A)PYRENE, MICE (1798)
 SOUTHERN IRAN, CANCER INCIDENCE (2041)
- SPLEEN
 EHRLICH ASCITES TUMOR, IMMUNITY, MICE (1999)
 FOLLICULAR LYMPHOMA, HEPATOSPLENIC SCHISTOSOMIASIS MANSONI (2122)
 FRIEND VIRUS, DEFECTIVE, HELPER (1900)
 FRIEND VIRUS, IMMUNITY (1902)
 RETICULUM CELL SARCOMAS, ANTIGEN, AGE, MICE (2001)
 SPLENOMEGALY, HARVEY MURINE SARCOMA VIRUSES, HELPER VIRUS FUNCTIONS (1935)
- STILBESTROL
 MATERNAL THERAPY, VAGINAL ADENOCARCINOMA (1831)
- STOMACH
 GASTRIC CANCER, NITROSAMIDES (1819)
 GASTRIC ULCER, MALIGNANT CHANGE (2031)*
 N-METHYLUREA, N-METHYL-N-NITROSOUREA, RAT (1820)
 TUMORS, METHYLNITROSOUREA, METHYLNITROSOURETHAN (1823)
- STRUCTURE
 ACTIVITY RELATIONSHIP, MONONITROQUINOLINES, HUCKEL (1826)
- SUSCEPTIBILITY
 VIRUS, PATHOLOGICAL RABBIT TISSUE (1963)
- SYNDROME
 REYE'S, TOXIC REACTION IN MONKEYS, AFLATOXIN B1 (1777)
- TERATOGENESIS
 CHICK EMBRYOS, MYCOTOXINS (1779)
 DIMETHYLNITROSAMINE, TRANSPLACENTAL, RAT (1811)
- TESTES
 TUMORS, MALIGNANT TROPHOBLASTIC TERATOMA, TUMOR SPREAD (2116)
- TESTOSTERONE
 RADIATION, HEMATOPOIETIC REGENERATION (1848)
- THIOACETAMIDE
 RNA METABOLISM, LIVER (1775)
- THOROTRAST
 RADIATION, RETROMANDIBULAR DAMAGE, THOROTRASTOMA (1862)*
- THYMUS
 LYMPHOMA INDUCTION, DOSE RESPONSE, URETHAN (1829)
 PIKE, LYMPHOSARCOMA (2126)
 THYMECTOMY, VIRAL TUMORIGENICITY, HAMSTER (1961)
- THYROID
 MEDULLARY CARCINOMA, PRE-AMYLOID SUBSTANCE, AMYLOID STROMA (2111)
 PRECANCEROUS ALTERATIONS, GOITER, ADENOMA, HUMANS (2030)
- L-THYROXINE
 METHYLTHIOURACIL, 7,12-DIMETHYLBENZ-(A)ANTHRACENE, RAT (1790)
- TOBACCO
 CANCER, SPONTANEOUS PNEUMOTHORAX, EMPHYSEMA, HYPERSENSITIVITY (1834)
 CIGARETTE, TUMOR PROMOTION, INSECTICIDE (1793)
 CIGARETTE SMOKE, 3,4-BENZO(A)PYRENE, METABOLISM OF CARCINOGEN (1796)
 HUMAN PLACENTA, BENZO(A)PYRENE HYDROXYLATION (1799)
 HYPERPLASIA, FOCAL PROLIFERATION, LUNG, RABBIT (1833)
 LUNG CANCER, EPIDEMIOLOGY (1741)
 MOSAIC VIRUS, POLYPHENOLS, CARCINOGENICITY (1836)*
 MOSAIC VIRUS, POLYPHENOLS, SMOKING, CARCINOGENICITY (1837)*
 NEUTRAL FRACTION, BENZO(A)PYRENE, SKIN, MICE (1798)
- TRANSFORMATION
 ABORTIVE, POLYOMA VIRUS, BHK 21 (195)
 CELL, FOCUS FORMATION, AVIAN MYELOBLASTOSIS VIRUS (1891)
- TRANSMISSION
 TRANSPLANTATION TUMOR, CANINE MAST CELL TUMOR (2131)
 TRANSPLANTATION PASSAGE IN DOGS, GUINEA PIG, CANINE LYMPHOSARCOMA (2132)
 VERTICAL, LEUKOSIS-FREE CHICKENS, AVIAN LEUKOSIS VIRUS (1888)
- TRANSPLANTATION
 TUMOR, METASTASES, FREUND ADJUVANT, RAT (2022)*
- TRAUMA
 BONE, WHOLE BODY IRRADIATION, OSTEOGENIC SARCOMA, MOUSE (1863)*
- TUBERCULOSIS
 LUNG CANCER, FINLAND (2117)
- ULTRASTRUCTURE
 ACID CARBOHYDRATES, BLOOD LYMPHOCYTE CELL MEMBRANE, HUMAN LYMPHOID

- LEUKEMIA (2142)*
 BASAL CELL CARCINOMA, MELANIN, KERATINOCYTES (2106)
 CAT CELL CARCINOMA, ACTH SYNDROME (2103)
 CONNECTIVE TISSUE, LYMPHOMA, THYMOMA (2113)
 DIMETHYLNITROSAMINE, ADENOCARCINOMAS (1809)
 DIMETHYLNITROSAMINE, RENAL MESENCHYMAL TUMOR, RAT (1807)
 HEPATOMA, AZO DYE, RAT (1785)
 HERPESVIRUS, INFECTIVITY, REVIEW (1759)
 HEXON, CRYSTALS, ADENOVIRUS (1913)
 HUMAN EPIDERMIS, SUNLIGHT EXPOSURE (1855)
 LEUKEMIA, MYELO-MONOCYTIC, MONOCYTIC, HUMAN (2115)
 LEUKEMOGENIC AND SARCOMAGENIC VIRUSES, VIRUS, PARTICLES (1866)
 MYOEPITHELIAL CELLS, ROLE IN NEOPLASIA (2035)*
 PANCREATIC ISLET CELL ADENOMA (2105)
 RODENT SARCOMAS, MOLONEY MURINE SARCOMA VIRUS (1930)
 STICKER'S TUMOR, DOG (2107)
 STORAGE CELL, GAUCHER'S DISEASE, CHRONIC MYELOGENOUS LEUKEMIA (2110)
 SV40, STRUCTURAL PROTEINS (1953)
 TUMOR, PAROTID, PATHOGENESIS, HUMANS (2033)*
- RETER
 LEUKOPLAKIA, CALCULUS (2141)*
- RETHAN
 7,12-DIMETHYLBENZ(A)ANTHRACENE, GAMMA-IRRADIATION, HORMONE (1789)
 7,12-DIMETHYLBENZ(A)ANTHRACENE, IMMUNE RESPONSE IN RATS (1989)
 THYMIC LYMPHOMA INDUCTION, DOSE RESPONSE (1829)
- TERUS
 3-METHYLCHOLANTHRENE, EPIDERMIZATION, MICE (1804)
 RADIATION, CARCINOGENICITY, RAT (1846)
- AGINA
 ADENOCARCINOMA, MATERNAL STILBESTROL THERAPY (1831)
 CARCINOMA, INCIDENCE, CONSTITUTION (2034)*
- IRUS
 ADENOVIRUS, CRYSTALS, HEXON (1913)
 ADENOVIRUS, PORCINE LEUKEMIA, STRONTIUM 90 (1838)
 ADENOVIRUS 2, PROTEIN SYNTHESIS, METHIONINE INITIATION (1911)
 ADENOVIRUS 2, STRUCTURAL PROTEINS (1912)
 ADENOVIRUS 12, ANTIGEN, HELA CELL (1981)
 ADENOVIRUS 12, DEFECTIVE (1914)
 ADENOVIRUS 12, T ANTIGEN, ULTRAVIOLET, IRRADIATION (1978)
 ADENOVIRUS-SV40 HYBRIDS, SV40 ANTIGEN (1980)
 AVIAN LEUKOSIS, ANTIGENS, IMMUNE RESPONSE, CHICKEN (1964)
 AVIAN LEUKOSIS, RNA (1887)
 AVIAN LEUKOSIS, VERTICAL TRANSMISSION, LEUKOSIS-FREE CHICKENS (1888)
 AVIAN LEUKOSIS VIRUS MC29, PROPERTIES (1735)
 AVIAN MYELOBLASTOSIS, FOCUS FORMATION, CELL TRANSFORMATION (1891)
 AVIAN TUMOR, RNA, NUCLEOTIDE COMPOSITION, HYBRIDIZATION (1942)
 BAI AVIAN LEUKOSIS, RNA, TRANSMISSION OF MYELOBLASTOSIS (1890)
 BOVINE LYMPHOSARCOMA (1873)
 BOVINE LYMPHOSARCOMA, CYTOPATHIC EFFECT IN MIXED CELL CULTURE (1876)
 BOVINE LYMPHOSARCOMA, TRANSMISSION OF DISEASE (2129)
 BOVINE SYNCYTIAL, VIRUS INFECTION IN SEVERAL SPECIES (1875)
 C-TYPE PARTICLES, LEUKEMIC COW LYMPHOCYTES, BOVINE LYMPHOCYTOSIS (1877)
 C-TYPE PARTICLES, MAMMARY TUMORS, LEUKEMIA, RAT (1870)
 CANCER, IMMUNITY, REVIEW, RATS, MICE, BIRDS (1734)
 CELL SENSITIVITY, PATHOLOGICAL RABBIT TISSUE (1963)
 COMPARISON, BOVINE LEUKOTIC VIRUS-LIKE PARTICLES, FELINE LEUKOSIS VIRUS (1874)
 DNA, POLYMERASE, BIRD (1943)
 DNA, POLYMERASE, MC29 TUMOR (1892)
 DNA, POLYMERASE, RNA, MILK, HUMAN (1878)
 EPSTEIN-BARR, ANTIBODIES, BURKITT'S LYMPHOMA (1973)
 EPSTEIN-BARR, ANTIBODY TITERS, MACAQUE MONKEYS (1974)
 EPSTEIN-BARR, BURKITT'S LYMPHOMA, VIRUS ANTIBODY IN TAIWAN MONKEY (1972)
 EPSTEIN-BARR, BURKITT'S LYMPHOMA CELLS (1886)
 EPSTEIN-BARR, DNA, METAPHASE CHROMOSOMES (1881)
 EPSTEIN-BARR, DNA STIMULATION, LEUKOCYTE (1884)
 EPSTEIN-BARR, GROWTH OF TRANSFORMED LEUKOCYTES IN VITRO (1883)
 EPSTEIN-BARR, HUMAN LEUKEMIC CELLS (1882)
 EPSTEIN-BARR, LYMPHOBLASTOID CELL LINES, CYTOGENETICS (1885)
 EPSTEIN-BARR, TUMOR MEMBRANE ANTIGENS, BURKITT'S LYMPHOMA (1739)
 FELINE LEUKEMIA, CHARACTERIZATION (1894)
 FELINE LEUKEMIA, GROUP-SPECIFIC ANTIGEN (1975), (1977)
 FELINE LEUKEMIA, GROWTH IN HUMAN CELLS (1895)
 FRIEND, BACTERIAL ANTIGENS, REPLICATION OF VIRUS (1899)
 FRIEND, DEFECTIVE, SPLEEN, ANTISERA (1900)
 FRIEND, SPLEEN, LEUKEMIA, RADIATION (1898)

FRIEND, SPLEEN CELLS, IMMUNITY (1902)
 FRIEND DISEASE, MYCOBACTERIUM BOVIS,
 IMMUNITY (1903)
 FRIEND LEUKEMIA, SPLEEN NUCLEOSIDE
 DEAMINASE ACTIVITY, MOUSE (1901)
 FUJINAMI ROUS SARCOMA, CELL MEMBRANES,
 MUCOPOLYSACCHARIDE LAYER (1948)
 GROSS, BITTNER, INTERFERENCE, MOUSE
 (1928)
 GROSS, LEUKEMOGENESIS, CHROMOSOMES
 (1904)
 GROSS LEUKEMIA, IMMUNOLOGY, GENETICS
 (1970)
 HARVEY MURINE SARCOMA, HELPER VIRUS
 FUNCTIONS, SPLENOMEGALY (1935)
 HERPES, GENITAL ORGANS, CANCER,
 REVIEW (1755)*
 HERPES, INFECTIVITY, CHEMICAL
 CONSTITUTION OF VIRUS, REVIEW (1759)
 HERPES SIMPLEX, BURKITT'S LYMPHOMA
 CELLS, GROWTH (1923)
 HERPES SIMPLEX, CHROMOSOMES, L CELLS,
 HEP2 (1921)
 HERPES-TYPE, GUINEA PIG LEUKEMIA
 (1920)
 HERPES-TYPE, HUMAN PERIPHERAL BLOOD,
 LEUKEMIA (1925)
 HERPES-TYPE, NASOPHARYNGEAL CARCINOMA,
 BURKITT'S LYMPHOMA (1922)

 HERPESVIRUS SAIMIRI, INTERFERON,
 POLY I.C (1918)
 HERPESVIRUS SAIMIRI, MALIGNANT
 LYMPHOMA, MONKEYS (1917)
 HERPESVIRUS SAIMIRI, PLAQUE FORMATION
 (1919)
 HERPESVIRUS TYPE 2, CERVICAL
 CARCINOMA, ANTIBODIES (1924)
 HUMAN LEUKEMIC CELLS, INDUCTION OF
 LEUKEMIA, MONKEYS (1867)
 HUMAN SARCOMAS, ANTISARCOMA ANTIBODIES
 (1880)
 LACTIC DEHYDROGENASE-ELEVATING VIRUS,
 POTENTIATION OF TUMORIGENICITY,
 MURINE SARCOMA VIRUS (1933)
 LEUKEMIA ANTIGEN, SUPPRESSION OF TUMOR
 GROWTH, IMMUNE LYMPHOCYTES (1969)
 LEUKEMOGENIC, GUINEA PIG LEUKEMIA
 (1871)
 LEUKEMOGENIC, SARCOMAGENIC, ULTRA-
 STRUCTURE (1866)
 MAMMARY TUMOR, CELL FUSION, IMMUNO-
 FLUORESCENCE STUDY, MURINE (1926)
 MAMMARY TUMORS, RNA, ANTIGEN CROSS-
 REACTION (1927)
 MAREK'S DISEASE, AGENT, CHICKEN EMBRYO
 (1915)
 MAREK'S DISEASE, CHICKEN FEATHER
 FOLLICLES (1916)
 MAREK'S DISEASE HERPESVIRUS, VIRAL
 ANTIGENS IN CHICKEN FEATHER
 FOLLICLES (1965)
 MOLONEY LEUKEMIA, TRANSMISSION,
 CHROMOSOME (1905)
 MOLONEY MURINE SARCOMA, HARVEY MURINE
 SARCOMA, INDUCTION OF BONE TUMORS
 (1938)

MOLONEY MURINE SARCOMA, RODENT SARCOMA
 (1930)
 MOLONEY MURINE SARCOMA, TRANSFORMATION
 IN VITRO, KIDNEY CELL CULTURE (1937)
 MURINE LEUKEMIA, COMPLEMENT FIXATION,
 HEMAGGLUTINATION REACTION (1909)
 MURINE LEUKEMIA, HEMOGLOBIN SYNTHESIS,
 DBA/2J (1897)
 MURINE MAMMARY TUMOR, HUMAN BREAST
 CANCER, NEUTRALIZATION (1929)
 MURINE SARCOMA, DEFECTIVENESS (1936)
 MURINE SARCOMA, FELINE LEUKEMIA,
 ALTERATION IN CULTURE (1934)
 MURINE SARCOMA, TUMOR REGRESSION,
 NEW ZEALAND MICE (1932)
 MYELOBLASTOSIS, AVIAN, ANTIGEN (1967)
 MYELOCYTOMATOSIS, DNA POLYMERASE,
 INFECTED CHICK CELLS (1893)
 MYELOID LEUKEMIA, STAPHYLOCOCCUS,
 CHICK (1889)
 ONCOGENICITY, HERPES GROUP (1752)*
 PAPOVA, HAMSTER PAPILLOMAS, LYMPHOMA
 (1956)
 PARTICLES, SPONTANEOUS LYMPHOMAS,
 RADIATION, HAMSTERS (1868)
 PARTICLES IN GUINEA PIG LEUKEMIA,
 TRANSMISSION (1865)
 POLYOMA, BHK, GLYCOSYLTRANSFERASE
 ACTIVITY (1958)
 POLYOMA, BHK 21 (1959)
 POLYOMA, TRANSFORMED CELLS, GLYCO-
 PEPTIDES (1957)
 POLYOMA, TRNA, RAT (1962)
 RADIATION, IMMUNIZATION, LEUKEMIA
 (1968)
 RAUSCHER LEUKEMIA, CHANGES IN ENZYME
 ACTIVITY, LEUKEMIA (1907)
 RAUSCHER LEUKEMIA, DECREASED LEUKEMO-
 GENICITY IN CULTURE (1910)
 RAUSCHER LEUKEMIA, HIGH AND LOW
 LEUKEMOGENIC VIRAL VARIANTS (1908)
 RAUSCHER LEUKEMIA, TUMORIGENIC MOUSE
 CELLS, DECREASED TUMORIGENICITY
 (1906)
 RNA TUMOR VIRUSES, VIRION RNA SYNTHESIS
 (1940)
 ROUS, DEFECTIVE STRAIN, HELPER,
 CHICKEN EMBRYO (1947)
 ROUS SARCOMA, AVIAN LEUKOSIS IN
 PIGEONS, COMPLEMENT FIXING ANTIGEN
 (1966)
 ROUS SARCOMA, BACTERIA (1946)
 ROUS SARCOMA, CELL SURFACE GLYCOPRO-
 TEINS (1939)
 ROUS SARCOMA, CHICK EMBRYO FIBROBLASTS
 RIFAMPICIN (1944)
 ROUS SARCOMA, DNA POLYMERASE (1941)
 SARCOMA 180, ANTIGEN (1995)
 SHOPE FIBROMA, DNA, RK 13, LACK OF
 HOMOLOGY (1949)
 SIMIAN ADENOVIRUS 7, 7,12-DIMETHYL-
 BENZO(A)ANTHRACENE, TUMOR TRANSPLANT
 IMMUNITY (1982)
 SV40, CELL ASSOCIATION, RECOVERY
 (1955)
 SV40, DNA, RNA, CHINESE HAMSTER (1954)
 SV40, DNA, SUPERHELICAL, NICKEL (1951)

40, DNA SYNTHESIS, 3T3 (1952)
40, KIDNEY, STRUCTURAL PROTEINS
(1953)

40, MOLONEY, MOUSE OVA (1931)

40, POLYOMA, MURINE SARCOMA,
TRANSFER RNA METHYLASE (1950)

40, TUMOR IMMUNITY, HAMSTER (1979)

THYMECTOMY, TUMORIGENICITY, HAMSTER
(1961)

TUMOR INDUCTION IN MAMMALS, FELINE
FIBROSARCOMA (1872)

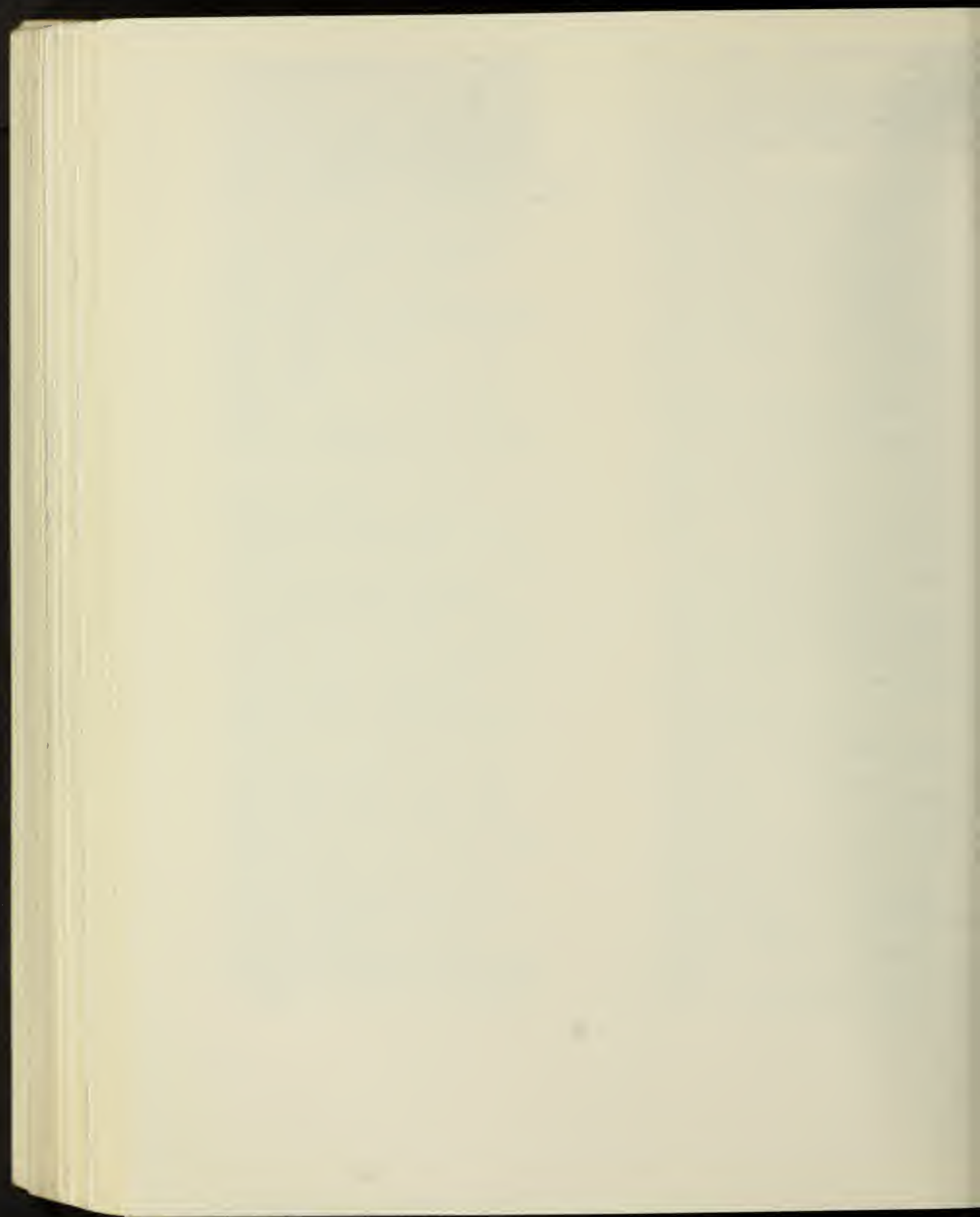
TYPE A PARTICLES, INTRACISTERNAL,
GERBIL FIBROMA (1869)

VACCINIA, HUMAN LYMPHOCYTES, CHROMO-
SOME ABERRATIONS (1879)

VIRAL REPLICATION, LATENT VIRUS (1733)

WART

ANTIGEN STUDIES, HUMAN (2017)





U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

OFFICIAL BUSINESS

PENALTY FOR PRIVATE USE, \$300



POSTAGE AND FEES PAID
U.S. DEPARTMENT OF H.E.W.

If you do not desire to continue receiving this publication, please CHECK HERE ☐:
tear off this label and return it to the above address. Your name will then be
promptly removed from the appropriate mailing list.

15
5
*Vet.
Med.*
MAY-JUNE 1971

Abstract Nos. 2146-2587

**Vol. 9
No. 11-12**

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health



CARCINOGENESIS ABSTRACTS

A monthly publication of the

National Cancer Institute

Editor

Robert Love, M.D.
Jefferson Medical College, Philadelphia

Associate Editor

George P. Studzinski, M.D.
Jefferson Medical College, Philadelphia

NCI Staff Consultants

Howard R. Rosenberg, M.S.
Sidney Siegel, Ph.D.
Elizabeth Weisburger, Ph.D.

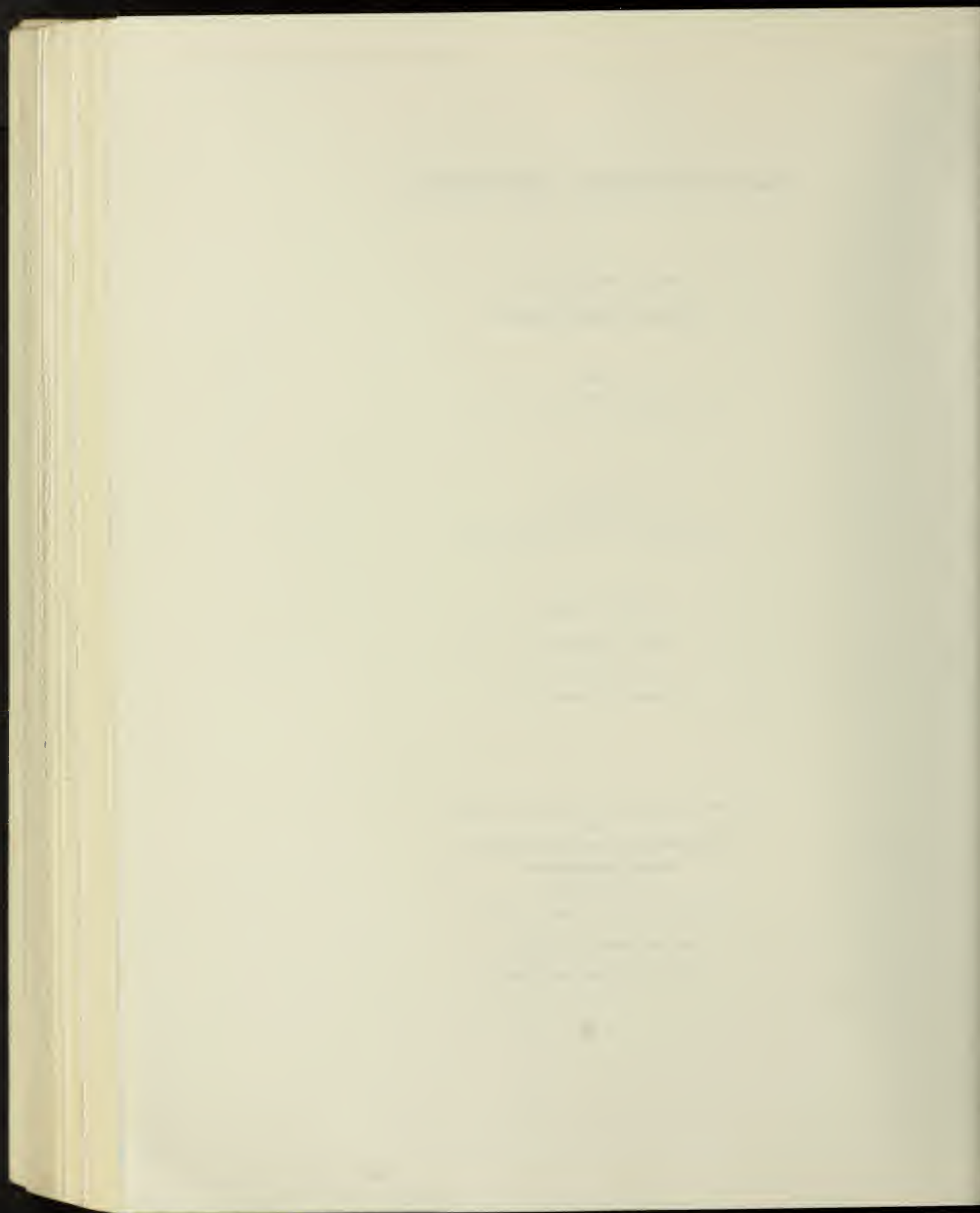
Literature Selected, Abstracted, and Indexed
by

The Franklin Institute Research Laboratories
Science Information Services
Biomedical Section

M. H. Fukami, Ph.D., Technical Editor

Contract Number NIH-71-2073

Public Health Service, USDHEW



PREFACE

Carcinogenesis Abstracts is a publication of the National Cancer Institute. The journal serves as a vehicle through which current documentation of carcinogenesis research highlights are compiled, condensed, and disseminated on a regular basis. It represents an integral part of the Institute's program of fostering and supporting coordinated research into cancer etiology. Issues of *Carcinogenesis Abstracts* normally contain two-hundred abstracts and twenty citations (unaccompanied by corresponding abstracts). Abstracts and citations refer to the current scientific literature that describes the most significant carcinogenesis research carried on at the National Cancer Institute, other governmental agencies, and private institutions. *Carcinogenesis Abstracts* is intended to be a highly useful current awareness tool for scientists engaged in carcinogenesis research or related areas. The great number and diversity of publications relevant to carcinogenesis make imperative the availability of this service to investigators whose work requires that they keep abreast with current developments in the field.

Carcinogenesis Abstracts is normally published monthly. Volume IX covers the scientific literature published from July 1970 through June 1971. A cumulative subject and author index for Volume IX will be published shortly after the final regular issue. This journal is available free of charge to libraries and to individuals who have a professional interest in carcinogenesis. Requests for *Carcinogenesis Abstracts* from qualified individuals should include statements of their relationship to carcinogenesis research. All correspondence should be addressed as follows:

Carcinogenesis Abstracts
Etiology Area
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20014

Use of Funds for Printing this publication
approved by the Director of the Bureau of
the Budget on July 25, 1967.

1.

2.

3.

4.

5.

6.

7.

8.

9.

10.

11.

12.

13.

14.

15.

16.

17.

18.

19.

20.

21.

22.

23.

24.

25.

26.

27.

28.

29.

30.

31.

32.

33.

34.

35.

36.

37.

38.

39.

40.

41.

42.

43.

44.

NOTE

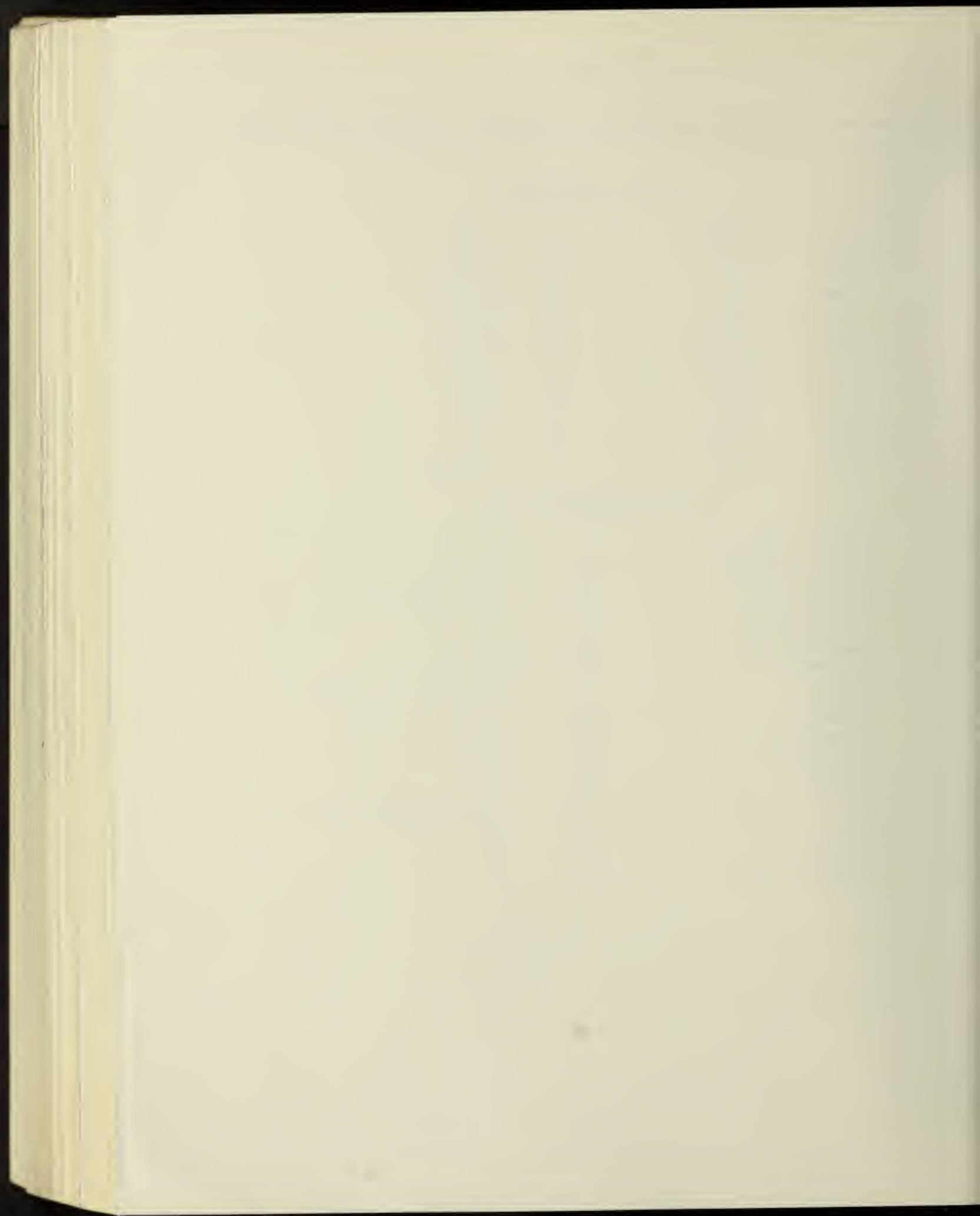
Journal names are abbreviated according to the list of abbreviations used by *Index Medicus*. For journals not covered by *Index Medicus*, the abbreviations (with some modifications) found in *World Medical Periodicals*, 3rd Edition, are used.

LANGUAGE ABBREVIATIONS

Afr.	Afrikaans	It.	Italian
Ar.	Arabic	Jap.	Japanese
Bul.	Bulgarian	Kor.	Korean
Ch.	Chinese	Latv.	Latvian
Cz.	Czech	Lith.	Lithuanian
Dan.	Danish	Nor.	Norwegian
Dut.	Dutch	Pol.	Polish
E.	English	Por.	Portuguese
Eston.	Estonian	Rum.	Rumanian
Fin.	Finnish	Rus.	Russian
Fl.	Flemish	Ser.	Serbo-Croatian
Fr.	French	Sl.	Slovak
Ger.	German	Sp.	Spanish
Gr.	Greek	Sw.	Swedish
Heb.	Hebrew	Th.	Thai
Hun.	Hungarian	Turk.	Turkish
Ic.	Icelandic	Uk.	Ukrainian
Ind.	Indonesian	Viet.	Vietnamese

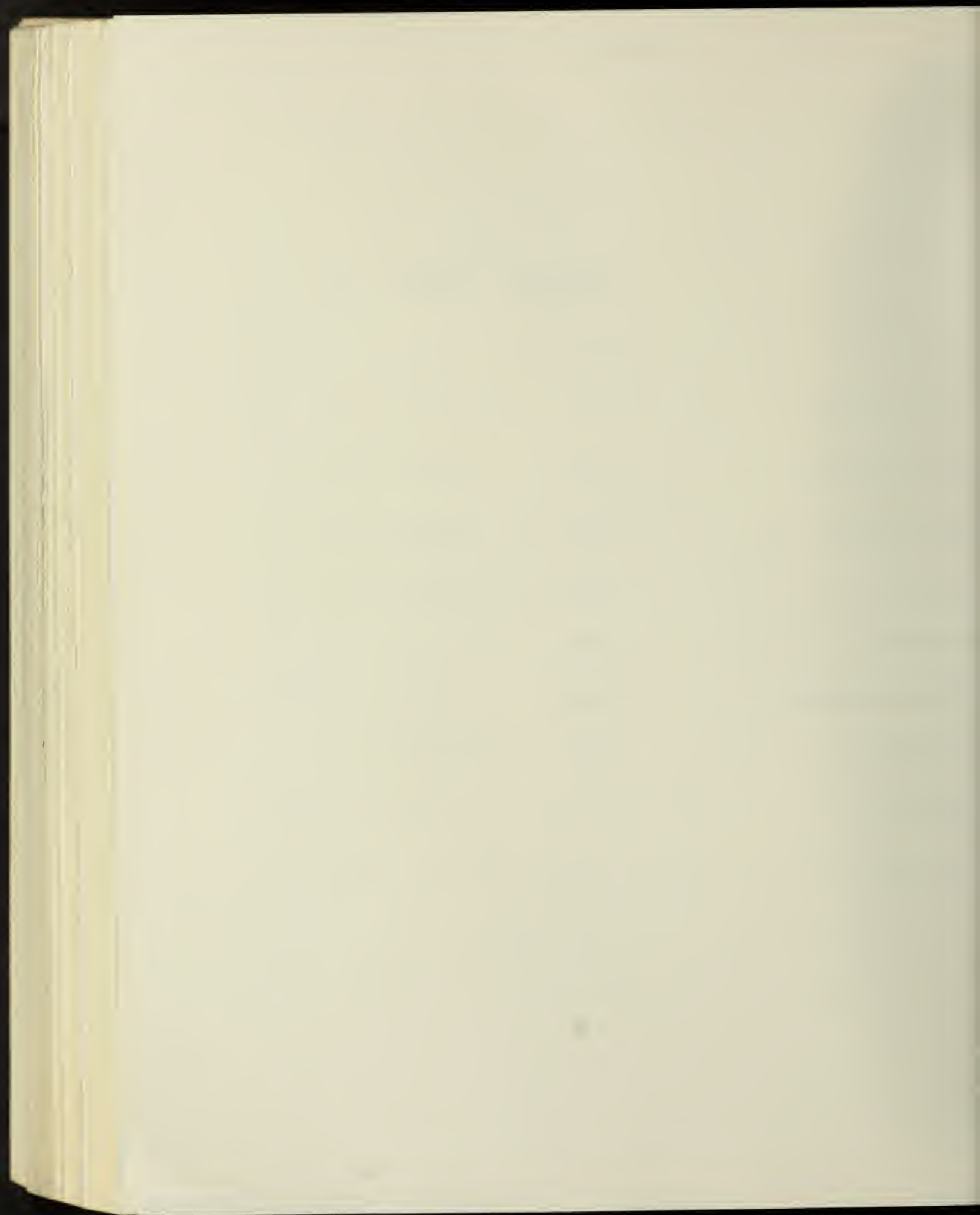
ABBREVIATIONS USED IN ABSTRACTS

ACTH	adrenocorticotrophic hormone	mg	milligram(s)
ADP	adenosine diphosphate	min	minute(s)
AMP	adenosine monophosphate	ml	milliliter(s)
ATP	adenosine triphosphate	mm	millimeter(s)
C	degrees centigrade	MTD	maximum tolerated dose
cm	centimeter(s)	ng	nanogram (10^{-9})
CNS	central nervous system	pg	picogram (10^{-12})
cpm	counts per minute	p.o.	orally
DNA	deoxyribonucleic acid	ppm	parts per million
e.g.	for example	r	Roentgen
g	gram(s)	RBC	red blood cells (erythrocytes), red blood count
ug	microgram(s)	resp.	respectively
hr	hour(s)	Rev.	review (only in citations)
i.m.	intramuscular	RNA	ribonucleic acid
i.p.	intraperitoneal	s.c.	subcutaneous
IU	international unit(s)	sec	second(s)
i.v.	intravenous	U	unit(s)
kg	kilogram(s)	UV	ultraviolet
LD ₅₀	median lethal dose(s)	WBC	white blood cells (leukocytes), white blood count
m	meter(s)	wk	week
M	molar	wt	weight
mEq	milliequivalent(s)	yr	year(s)
mM	millimolar		
uM	micromolar		
mC, μ C	milli-,microcurie(s)		



CONTENTS

	Cross Reference Abbreviations	Abstracts, Citations	Page
REVIEW	(Rev)	2146-2177	471
CHEMICAL CARCINOGENESIS.	(Chem)	2178-2273	476
PHYSICAL CARCINOGENESIS.	(Phys)	2274-2294	496
VIRAL CARCINOGENESIS.	(Viral)	2295-2400	501
IMMUNOLOGY.	(Immun)	2401-2466	523
PATHOGENESIS.	(Path)	2467-2478	539
EPIDEMIOLOGY AND BIOMETRY.	(Epid-Biom)	2479-2499	542
MISCELLANEOUS.	(Misc)	2500-2587	547
AUTHOR INDEX.			i
SUBJECT INDEX.			xiii



REVIEW

6 THE ALKYLATION OF TRANSFER RNA BY ENZYMES FROM EMBRYONIC, NEOPLASTIC, AND ETHIONINE-INDUCED LIVER TISSUES. (E.) Hancock, R. L. (Fac. of Medicine, U. Calgary, Alberta, Canada). *Cancer Res* 31(5):620, 1971.

Recent experimental findings concerning aspects of the alkylation of tRNA were reviewed. High molar concentrations of mono- and divalent cations (e.g., 0.2-0.5 M of ammonium ion and 0.01 M of magnesium ion) have been found to enhance tRNA methylase activity; it has been suggested that this enhancing effect on tRNA is due to alterations in the conformation of tRNA. Investigations of 2'-O-methylase activity in liver and hepatoma extracts have shown that tumor tissue extracts methylate tRNA in 2'-O positions. In studies to determine the required substrate characteristics of tRNA methylases it has been found that tRNA methylases do not methylate homopolymers (including polyuridylic, uridylic, guanylic and cytidylic homopolymers). tRNA methylases, however, were able to methylate short fragments of *E. coli* tRNA. Continuing studies have suggested that adult and embryonic cells contain different forms of leucyl-tRNAs and that hepatoma enzymes, when compared with normal liver enzymes, preferentially methylate some *E. coli* tRNAs. Mice fed diets containing 1% ethionine showed an 80% increase in liver tRNA methylase activity compared to mice given a conventional diet. It has been hypothesized that all carcinogenic phenomena may be the result of alterations of minor nucleotides in tRNA; such alterations could affect the genetic information encoded on the DNA of new cells. (41 references)

7 SUMMARY OF SYMPOSIUM ON TRANSFER RNA AND TRANSFER RNA MODIFICATION IN DIFFERENTIATING AND NEOPLASIA. (E.) Zamecnik, P. C. (Massachusetts Gen. Hosp., Boston). *Cancer Res* 31(5):716-720, 1971.

Review of the literature on biochemical characterization of tRNAs, alterations of tRNA during differentiation, and alterations in tRNA and tRNA methylation in neoplasia is presented. I. Base modifications of tRNA such as methylation are believed to change tertiary structure of the tRNAs and to modulate several functions. Data from several experiments indicate the anticodon in amino acid recognition as well as in the established interaction with the codon of mRNA. Evidence points to the dihydrouracil loop as being essential for aminoacyl synthetase recognition. Undermethylated tRNA cannot be aminoacylated as well as normally methylated tRNA. Overmethylated tRNA, and its circular dichroic and optical rotary dispersion pattern and melting profile differ from fully methylated tRNA. II. Evidence indicates that there are more isoacceptor tRNA species in embryonic forms of a tissue than in adult tissue. It is believed that differentiation and loss of synthetic capacities characteristic of cell growth are associated with loss of specific isoacceptor tRNA species, with consequent codon restriction. III. Methylase activity and methylation patterns appear to be more nearly alike between neoplastic and fetal tissue than between fetal and adult tissues. Studies relating chemical methylation to carcinogenesis con-

cluded that while there is no clear indication of which bases of nucleic acids are critical for carcinogenesis, tRNA may be a crucial target. No conclusion was reached on whether all carcinogenesis might be due to alterations of minor bases of tRNA. With the recognition of the Temin-Baltimore enzyme, the idea of some normal feedback from tRNA to the genetic material may not be as remote as first thought. (87 references)

2148 STUDIES ON GENETICALLY ALTERED RNA SPECIES IN *Escherichia coli*. (E.) Carbon, J. (Dept. Biol. Sci., U. California, Santa Barbara) and C. Squires. *Cancer Res* 31(5):663-666, 1971.

Recent investigations of *E. coli* tRNAs altered by mutation were reviewed; experimental work has concentrated on bacterial strains bearing suppressor mutations which revert various missense mutations in the gene specifying the tryptophan synthetase A protein. The A protein mutations, A36, A58 and A78 involve the replacement of specific glycine residues by other amino acids, resulting in an inactive enzyme. The mutations induced codon changes in the A protein message. Specifically, 4 suppressor mutations were listed which resulted in the presence of tRNAs capable of accepting glycine and of inserting it into peptide linkage in response to the altered codon. As an example, the mutation designated *glyT-su36* resulted in a tRNA^{Gly} which could recognize the arginine codon. Some mutations were found to result in the disappearance of a portion of the tRNA; this disappearance produced pleiotrophic effects and was associated with incapability of mutant *E. coli* strains to divide normally on complex media. (12 references)

2149 ON THE INTERACTION OF CARCINOGENS WITH DNA. (E.) Brookes, P. (Chester Beatty Res. Inst., Inst. Cancer Res., Royal Cancer Hosp., London, England). *Biochem Pharmacol* 20(5):999-1003, 1971.

Carcinogen-DNA interaction is reviewed with respect to N-hydroxylation and esterification which are the probable activation steps preceding the binding of aromatic amine and amide carcinogens to protein; the production of 7-alkylguanine moieties in response to alkylating agents was also discussed. DNA binding, but not RNA or protein binding, correlates with tumor-initiating potency in the case of lactones. Carcinogenic hydrocarbons are metabolized to chemically reactive derivatives which bind to DNA, RNA and protein. The macromolecule which represents the vital target for tumor initiation is still in doubt, although there is a striking similarity in the nature of the metabolically produced ultimate carcinogen, despite the widely different classes of compounds considered. (32 references)

2150 THE POSSIBLE ROLE OF NUCLEIC ACID METHYLASES IN THE INDUCTION OF CANCER. (E.) Magee, P. N. (The Middlesex Hosp. Med. Sch., London, England). *Cancer Res* 31(5):599-604, 1971.

The role of aberrant nucleic acid methylases in the induction of cancer is reviewed. Increased levels

of tRNA methylases have been reported in a variety of tumor tissues and increased levels of methylated purines have been found in the urine of humans with leukemia and in the urine of tumor-bearing animals. In addition, the level of labeling of methylated bases in tRNA increases in animals fed carcinogenic diets. It is agreed among many investigators that the macromolecule must be the crucial cellular target, although compelling evidence for this is lacking. However, all major groups of chemical carcinogens either react directly or give rise to chemically reactive intermediates that react with DNA, RNA, and proteins; on the basis of recent experimentation, DNA has been favored as the most likely cellular target. Yet, lack of evidence for a change in DNA analogous to mutation and the apparent normality of tumor DNA together with the evidence that tumor cells can, in some circumstances, revert to normal cells provides a reason for preferring tRNA as the primary target for chemical carcinogens on the basis of its greater degree of methylation than other types of RNA in cancerous tissue. (59 references)

- 2151 THE EARLY INTERFERENCE OF LIVER CARCINOGENS WITH PROTEIN SYNTHESIS AND ITS POSSIBLE BEARING ON THE PROBLEM OF TUMOR INDUCTION. (E.) Hultin, T. (Wenner-Gren Inst., Stockholm, Sweden). *Biochem Pharmacol* 20(5):1001-1017, 1971.

The effect of liver carcinogens relative to tumor induction is reviewed. Cellular interaction may directly or indirectly affect the synthesis of cell proteins; thus nucleoli are particularly sensitive indicators of the early interference of carcinogens with nuclear functions. Several carcinogens give rise to partial segregation of particulate and fibrillar components of the nucleoli; moderate reduction is seen in the amount of 40-60 min pulse-labeled RNA in response to sublethal doses of CCl_4 , indicating decreased efficiency of nucleocytoplasmic RNA-transportation. Because of its great structural complexity the mitotic part of the cell cycle is particularly sensitive to injury which may lead to errors in the redistribution of genetic material and direct damage to DNA by reactive metabolites may contribute to carcinogenic effects. However, since the important functions of cell nuclei in regulation and differentiation are mediated through cytoplasmic processes also, neoplastic transformation is not necessarily an isolated nuclear phenomenon. (60 references)

- 2152 SUSCEPTIBILITY OF THE GUINEA PIG TO CHEMICAL CARCINOGENESIS. (E.) Argus, M. F. (USPHS Hosp., New Orleans, La.). *Cancer Res* 31(6):917-918, 1971.

Recent discoveries relative to the susceptibility of the guinea pig to chemical carcinogens were reviewed. It has been shown that guinea pigs are highly susceptible to the hepatocarcinogenic action of diethylnitrosamine, dimethylnitrosamine, di-n-butyl nitrosamine, methyl nitrosourea, cycad meal, methylazoxymethanol, aflatoxin and dioxan. Guinea pigs are resistant to carcinogenesis by aromatic amines and amino azo dyes, perhaps due to their limited ability to metabolize these compounds to their N-hydroxy derivatives. It has been shown that guinea pigs treated with N-

hydroxy-2-acetylaminofluorene developed adenocarcinomas in the small intestine, while 2-acetylaminofluorene was inactive. (31 references)

- 2153 RELATIONSHIPS BETWEEN ELECTRONIC TRANSFER ENERGIES, CARCINOGENIC ACTIVITY AND HYDROPHOBIC BINDING TO PROTEIN OF POLYCYCLIC AROMATIC HYDROCARBONS. (Ger.) Franke, R. (Chem. Sec., T. U. Dresden, Germany) and M. Büchner. *Arch Geschwulstforsch* 37(1):45-52, 1971.

Highly significant linear correlations between electron transfer energies ΔE_1 and ΔE_2 and the carcinogenic activity of polycyclic aromatic hydrocarbons were found using experimental data available from the literature. However, these statistical correlations did not allow the prediction of carcinogenic activity for single hydrocarbons. The shortcoming was assumed to be due to other factors such as hydrophobic binding between hydrocarbon and protein which interfered in the mechanism of carcinogenic activity. An analysis of previously obtained aromatic hydrocarbon-protein binding data (with human serum albumin) and carcinogenic activity revealed a relationship that did not affect the correlations between carcinogenic activity and electron transfer energies. Thus the hydrophobic hydrocarbon-protein complex formation could not be considered as a possible secondary interference factor. Therefore the chemical reactivity of the single hydrocarbons rather than the electron transfer energies should be considered the primary factor in their carcinogenicity. (46 references)

- 2154 METAL CARCINOGENESIS IN EXPERIMENTAL ANIMALS. (E.) Sunderman, F. W., Jr. (U. Conn. Sch. Med., Hartford). *Fd Cosmet Toxicol* 9(1):105-120, 1971.

Recent literature dealing with the carcinogenic effects in animals of nickel, beryllium, cadmium, chromium, cobalt, iron, lead, selenium, zinc and titanium compounds was reviewed. Compounds containing beryllium have been shown to cause osteosarcoma in rabbits when administered i.v. Cadmium compounds cause sarcomas and interstitial cell tumors of the testis in chickens, rats and mice when injected or s.c. Special emphasis was given to the literature of nickel carcinogenesis; compounds containing the element have been shown to cause sarcomas, squamous cell carcinomas and anaplastic carcinomas in rats, rabbits, and guinea pigs, when administered by inhalation, i.m., or by an intrapulmonary route. Little evidence was found in the literature to support the hypothesis that metallic compounds present in food cause cancer in man. (170 references)

- 2155 REVERSION IN CELLS TRANSFORMED BY TUMOR VIRUSES. (E.) Macpherson, I. A. (Imperial Cancer Res. Fund Lab., London, England). *Proc Soc Lond* 177(1046):41-48, 1971.

The transformation of animal cells by DNA and tumor viruses was discussed, with special reference to the phenomenon of "reversion" of cell transformation, in which transformed cells lose their virus-transformed characteristics. In some cases of

version, the transformed cells seem to lose the viral genes entirely; loss may occur spontaneously, as in the loss of the Rous sarcoma virus genome by transformed baby hamster kidney cells, or loss may be induced by chromosome loss in the transformed cells, as in the reversion of polyoma virus infection in transformed baby hamster kidney cells. In other instances of reversion, the viral genes remain in the transformed cells, but in an inactivated state, as in the conditional lethal mutants of polyoma virus and avian sarcoma virus. Reversion can be induced by culturing transformed cells on formaldehyde; polyoma virus-transformed hamster cells lose some of their transformed properties in these circumstances. Reversion may also be accomplished by killing transformed cells with fluorodeoxyuridine or bromodeoxyuridine and light. Transformed cells treated with these agents have been shown to lose some of the characteristics of virus-transformed cells, at least temporarily. (25 references)

66 THE VIRAL GENOME IN TRANSFORMED CELLS. (E.) Berg, P. (Stanford U. Sch. Med., Calif.). *Proc Roy Soc Lond* 177(1046):65-76, 1971.

Evidence establishing the presence of viral genes in virally-transformed cells is reviewed. The hypothesis that transformed cells contain the viral genome, initially suggested by the discovery of clear and transplantation antigens in cells infected with DNA tumor viruses, has been confirmed by A-DNA hybridization experiments showing that polyoma virus-transformed cells contain an RNA fraction which is homologous to polyoma virus DNA. Viral DNA has also been demonstrated in virally-transformed cells, and the evidence is that transformed cells contain the whole viral genome. Viral DNA has been shown to be confined to the nuclei of transformed cells. Recent experiments with 3T3 mouse cells transformed with a thermosensitive strain of polyoma virus have suggested that the induction of viral multiplication in transformed cells involves the synchronous occurrence of a unique event, after which DNA synthesis can continue even under non-permissive conditions. In the experiments with polyoma virus, it was also shown that superhelical closed circular dimers and trimers of viral DNA were synthesized as were monomeric molecules; the oligomers amounted to up to 40% of viral DNA. One possible explanation for the formation of large quantities of polyoma oligomers following activation of the thermosensitive strain of polyoma virus in 3T3 cells is that the polyoma genome is integrated into the host-cell chromosomal DNA, where several viral DNA replicons are ordered in tandem at various chromosomal sites. (17 references)

67 SV40 SPECIFIC 'REPRESSOR' IN INFECTED AND TRANSFORMED CELLS. (E.) Cassingena, R. (Cancer Res. Inst., Villejuif, France) and P. Burnier. *Proc Roy Soc Lond* 177(1046):77-85, 1971.

Recent experiments were reviewed which demonstrated that non-permissive SV40-transformed cells contain

a protein which inhibits viral plaque formation in permissive cells. Extracts of SV40-transformed hamster, mouse, or cat cells inhibited plaque formation by SV40-infected monkey cells when the extract was added to the monkey cells with a basic polymer such as poly-L-lysine. Plaque formation inhibition was not seen in cells treated with extracts of normal or spontaneously transformed cells, cells transformed by 3-methylcholanthrene, adenovirus, or polyoma virus. In cells treated with extracts from non-permissive cells, inhibition of plaque formation attained 30-50%. It was found that the plaque formation-inhibiting protein (designated an SV40-specific "repressor") was present in abortive as well as in productive virus infections; however, in productive infections, the repressor was present in reduced amounts only. When extracts of repressor-containing SV40 cells were mixed with extracts of uninfected permissive cells, no inhibition of plaque formation was seen. (11 references)

2158 IMMUNOLOGICAL STUDIES ON A HUMAN TUMOR. DILEMMAS OF THE EXPERIMENTALIST. (E.)

Klein, G. (Inst. Tumor Biol., Karolinska Inst., Stockholm, Sweden). *Israel J Med Sci* 7(1):111-131, 1971.

A review of immunological studies on Burkitt's lymphoma is presented. Fresh Burkitt's lymphoma biopsy cells were exposed to the sera of Burkitt's lymphoma patients and various other donors in an attempt to isolate attached immunoglobulins by the indirect membrane fluorescence technique. The sera reacted more frequently than control sera from donors with other neoplastic or non-neoplastic diseases; most regularly positive sera were derived from patients whose tumors had gone to total regression after chemotherapy. Lymphoma cells, but not bone marrow cells, from the same allogeneic Burkitt's lymphoma donor, reacted regularly, increasing the probability that reactivity was not due simply to the presence of isoantibodies. A variable degree of immunoglobulin coating on the surface of the biopsy cells was of 2 basically different kinds, IgM or IgG or both, and these showed not only a difference in class specificity but also a difference in behavior in relation to the course of the disease; the IgG coat was rarely present in untreated biopsy cells and tended to appear only if the tumor persisted in spite of treatment. Four Burkitt's lymphoma-derived cell lines gave positive membrane immunofluorescence reactions in the indirect test after exposure to the reference serum derived from a patient in long-term regression; 8 controls from normal or leukemic patients were negative. Positively reacting cells revealed the presence of EBV-antigens in more than 1% of the cells compared to less than 1% in the negatively-reacting cells. Whether Epstein-Barr virus-associated membrane antigens are essential for the neoplastic behavior of Burkitt's lymphoma is not clear. (129 references)

2159 IMMUNOLOGICAL FACTORS IN NONSPECIFIC STIMULATION OF HOST RESISTANCE TO SYNGENEIC TUMORS: A REVIEW. (E.) Yashphe, D. J. (Dept.

Immun., Hebrew U. Hadassah Med. Sch., Jerusalem, Israel). *Israel J Med Sci* 7(1):90-107, 1971.

The nonspecific immunogenic potential of endotoxins, mycobacterial moieties and other microbial substances based on clinical observations is discussed. *Corynebacterium parvum* has recently been found to have tumor resistance-inducing properties in experimental animals and *Bordetella pertussis* gives evidence of prolonging remissions of acute leukemia in man. An active methanol extraction residue of BCG has been shown to inhibit malignant tumors, and DNA digests have decreased the incidence or delayed the appearance of spontaneous tumors in mice. Stimulation of immunogenicity before tumor challenge appeared to provide greatest resistance; although there is no direct evidence that these materials stimulate a specific immune response to tumors, it is assumed that elevated host resistance is brought about by an elevated immune response based on observations that tumors are immunogenic and immunization of isogenic hosts protects against subsequent challenge with a graft of the same or of a cross-reacting tumor. That suppression of immune response may be a necessary condition for tumor induction is indicated by the immunosuppressive action of a number of potent carcinogenic hydrocarbons as well as such moieties as antithymocyte serum and anti-lymphocyte serum which can cause increased incidence of tumor formation or leukemia in mice. In addition, specific immunological tolerance to tumor antigens has been suggested as one important factor in the low level of host responsiveness to autochthonous tumors. Immunity to tumors appears to reside largely in populations of lymphoid cells and substances which stimulate tumor resistance also affect either antibody formation or cellular immunity. There may be a variety of cellular functions which can be triggered by non-specific stimulators in place of antigen. (128 references)

- 2160 IMMUNOLOGICAL ASPECTS OF THE RELATIONSHIP BETWEEN HOST AND ONCOGENIC VIRUS IN THE MOUSE MAMMARY TUMOR SYSTEM. (E.) Blair, P. B. (Dept. Bacteriol., U. California, Berkeley). *Israel J Med Sci* 7(1):161-186, 1971.

The immunological response to mammary tumor virus in the mouse is reviewed. Although the neonatally infected mouse is at least partially tolerant to the antigens of the virion and of the infected cells, both noninfected and infected animals are capable of responding immunologically to mammary tumor virus-associated antigenicity. There is some evidence that an infected female mouse which is genetically resistant to the virus may transmit resistance factors to her offspring, but genetically susceptible mice apparently do not produce such resistance factors. Protection against the development of challenge isografts can occur with adoptive transfer of lymphoid cells and transfer of serum antibody from immunized infected mice. Many attempts to immunize infected mice against mammary tumors have resulted, however, in acceleration of tumor growth rather than repression; since the dominant component in immunological protection against solid tissues containing foreign antigens is cell-

associated and not humoral, the approach to immunotherapy should be concerned with evoking cell-associated immunological responses by immunization with membrane bound antigens. An appropriate immunization with inactivated and similar but not identical virus might induce an immunologic response in the host which would be effective against its own virus-induced plasm. (96 references)

- 2161 THE ROLE OF SOME ENDOCRINE GLANDS IN THE PATHOGENESIS OF HORMONE-PRODUCING TUMORS OF THE ADRENAL CORTEX. (Rus.) Sudarev, P. V. (Inst. Exper. Endocrinol. Acad. Med. Sci. U.S.S.R.) and V. I. Kertsman. *Vop Onkol* 17(2):102-107, 1971.

The disruption of the hormonal equilibrium as a factor in the pathogenesis of hormone producing tumors is reviewed. The functional relationship between the hypothalamus, adrenal cortex and gonads is reflected by the morphological alterations occurring in the hypothalamus and adrenal cortex following gonadectomy. Ovariectomy results in an increased gonadotropic stimulation of the adrenal cortex (compensatory action) which leads to the production of adrenal androgens which have different characteristics from the ovarian estrogens. The carcinogenic effect of these hormones is assumed to consist of a long term alteration of the relationship between the proliferative and secretory processes within the tissues subjected to hormonal stimulation. (62 references)

- 2162 MALIGNANT TUMOR OF THE NASOPHARYNX: REVIEW OF LITERATURE, AND OBSERVATION OF 100 CASES (1942-1965). (E.) Hara, H. J. (Loma Linda Univ. Los Angeles, Calif.) *J Otolaryng Soc Aust* 3(2):187-188, 1971.

Nasopharyngeal carcinoma may appear at an early age. 6 of 100 cases observed in the present series occurred in people under 30-yr-old; the condition is more frequent in males than in females, 73 males and 27 females comprising the series. The most common affected age group was the 51-60-yr-old group. The established predilection of the Chinese for nasopharyngeal carcinoma was borne out by the present investigation; 18 cases occurred among Chinese people, making them the second most commonly affected group (after 57 Caucasian cases). Other populations which have been shown to have an unusually high incidence of nasopharyngeal cancer are Kenyan and Malayan Indonesians. While the carcinogenic factors associated with nasopharyngeal carcinoma remain to be elucidated, environmental factors such as irritating dust, fumes, and unsanitary living conditions, are thought to be implicated in the origin of the condition. Of the 100 cases reviewed, 58 were classified as squamous cell carcinoma and 27 as anaplastic carcinoma; most nasopharyngeal tumors are of epidermoid origin. Other less frequently encountered histologic types of tumor were lymphoepithelioma, transitional cell carcinoma, reticular cell sarcoma and lymphosarcoma and adenocystic carcinoma. The prognosis for patients with nasopharyngeal cancer is usually poor, partly for the

on that the condition may remain without overt
ptoms until it has reached an advanced stage.
references)

ROLE OF MYOEPIHELIAL CELLS IN THE DEVELOP-
MENT OF SALIVARY GLAND TUMORS. (E.)
er, G. (Inst. Path., U. Köln, Germany), H. J.
n, O. Kleinsasser and H. G. Schiefer. *Cancer*
) :1255-1261, 1971.

Structural investigations concerning the role
of myoepithelial cells in the growth and structure
of salivary duct carcinomas, salivary gland cylindro-
and pleomorphic adenomas (e.g., "mixed tumors")
of the salivary gland were reviewed. In the duct
carcinoma, myoepithelial cells appear to be intact,
and grow together with epithelial cells. In the
adenoma, myoepithelial cells produce increased
amounts of interstitial material and this, together
with a loosened connection with epithelial cells,
leads to a cribriform pattern and a slower growth
rate than is seen in the duct carcinoma. In the
duct tumor the overproduction of interstitial
material by myoepithelial cells leads to a slow and
atypically benign tumor growth rate. Myoepithelial
cells and elements have also been discerned in those
salivary gland tumors which contain oncocytes:
adenoma lymphomatosum (e.g., "Whartin's" tumor)
and oncocytoma. (16 references)

INTERACTIONS OF ONCOGENIC VIRUSES AND ANI-
MAL CELLS. (E.) Yoshikawa-Fukada, M. (Inst.
of Res., Kyoto U., Japan) and J. D. Ebert. *Bio-
science* 21(8):357-366, 1971. (106 references)

THE PATHOLOGY OF TUMORS: I. INTRODUCTION,
PRECANCEROUS LESIONS, BENIGN LESIONS THAT
LEAD TO CANCER. (E.) Ackerman, L. V. (Washington
Univ. Sch. Med., St. Louis, Mo.) and J. Rosai. *Cancer*
for Clinicians 21(3):163-173, 1971. (22 references)

SPREAD OF AVIAN LEUKEMIA GROUP VIRUSES AND
METHODS OF THEIR IDENTIFICATION. (Rus.)
Nin, E. S. (Exp. Biol. Models Res. Lab. Acad.
Sci. U.S.S.R., Moscow), V. A. Dushkin and I. I.
Bilov. *Vop Virus* (2):131-137, 1971. (71 refer-
ences)

EXPERIMENTAL TUMORS IN FISH. (Rus.) Khu-
doley, Y. V. (N.N. Petrov Res. Inst. Oncol.,
Novograd, U.S.S.R.). *Vop Onkol* 17(1):87-94, 1971.
(references)

2168 CARCINOGENESIS, THE ENVIRONMENT, AND GENE
ACTION. (E.) Gelboin, H. V. (Natl. Cancer
Inst., Natl. Inst. Hlth., Bethesda, Md.). *Radiology*
99(2):251-264, 1971. (18 references)

2169 MURINE SARCOMA VIRUS. (Rus.) Yakovleva,
L. S. (Inst. Exp. Clin. Oncol. Acad. Med.
Sci. U.S.S.R., Moscow). *Vop Virus* 16(1):3-9, 1971.
(66 references)

2170 PROLIFERATION OF MYELOID CELLS. (E.) Perry,
S. (Natl. Cancer Inst., Natl. Inst. Hlth.,
Bethesda, Md.). *Ann Rev Med* 22:171-184, 1971. (97
references)

2171 CANCER HAZARDS FROM SYNTHETIC SWEETENERS.
(Fr.) Rudali, G. (Lab. Genet. Curie Fdn.,
Paris, France). *Presse Med* 79(13):569-572, 1971.
(13 references)

2172 ANTIGENIC REVERSION IN HUMAN CANCER. (E.)
Gold, P. (McGill U. Clin. Montreal General
Hosp., Canada). *Ann Rev Med* 22:85-94, 1971.
(50 references)

2173 CANCER AND THE ENDOCRINE GLANDS. (Fr.)
Klotz, H.-P., Ed. (Expansion Scientifique
Francaise, Paris). *Problemes Actuels d'Endocrinolo-
gie et de Nutrition* Ser. No. 13, Oct. 24-25, 1969.
(references)

2174 HUMAN CHROMOSOME DAMAGE BY CHEMICAL AGENTS.
(E.) Shaw, M. W. (U. Texas Grad. Sch. Bio-
med. Sciences, Houston). *Ann Rev Med* 21:409-432,
1970. (16 references)

2175 CHROMOSOMAL ABNORMALITIES IN HUMAN NEOPLASIA.
(E.) Sandberg, A. A. (Roswell Park Memorial
Inst., Buffalo, N.Y.) and D. K. Hossfeld. *Ann Rev
Med* 21:379-408, 1970. (336 references)

2176 CARCINOGENIC COMPOUNDS IN FOODS. (Rus.)
Neyman, I. M. (Inst. Nutr. Acad. Med. Sci.,
Moscow, U.S.S.R.). *Vop Pitan* 1:24-31, 1971. (80
references)

2177 GENETIC ASPECTS OF CARCINOGENESIS. (E.)
Zimmermann, F. K. (Forestry Inst., U.
Freiburg, Germany). *Biochem Pharmacol* 20(5):985-995,
1971. (93 references)

2178 INTERACTION OF DNA WITH THREE DIMETHYL DERIVATIVES OF BENZ(c)ACRIDINES. (E.)

Chan, E. W. (Cancer Res. Lab., U. Western Ontario, London, Canada) and J. K. Ball. *Biochim Biophys Acta* 238(1):31-45, 1971.

The product which resulted from a mixture of highly polymerized calf thymus DNA solution and a solution of dimethylbenz(c)acridine was analyzed for sedimentation determination, calculation of the binding ratio, and thermal denaturation. The extent of binding for the 7,9-derivative reached a level corresponding to a maximum binding ratio of 1 mole to 16 moles of DNA phosphate; similar results were obtained with the 7,10-derivative, whereas the binding ratio of the 7,11-derivative was about 1 mole to 82 moles of DNA phosphate. With the 7,10-derivative, binding was enhanced 4-fold when the pH was lowered from 8 to 6 and the ratio of un-ionized: ionized 7,10-derivative decreased by a factor of 250; high ionic strength inhibited binding which decreased almost 4-fold when the concentration of NaCl in the standard binding buffer was raised from 10^{-3} to 10^{-2} M. Similarly, the divalent Mg^{2+} and Mn^{2+} cations were more effective in inhibiting binding than were the monovalent cations. The binding of 7,10-dimethylbenz(c)acridine to DNA stabilized the DNA against heat denaturation and lowered the sedimentation rate of the DNA in sucrose gradients. The spectral characteristics of the binding to native and to denatured DNA were qualitatively and quantitatively the same and indicated that the mode of binding of the 7,10-derivative to the 2 forms of DNA was identical.

2179 STUDIES ON THE EFFECTS OF CHEMICALS ON THE PROCESSING OF NUCLEAR RNA: SOME POSSIBLE IMPLICATIONS WITH RESPECT TO CARCINOGENESIS. (E.)

Sporn, M. B. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *Biochem Pharmacol* 20(5):1029-1033, 1971.

A hypothesis is advanced for the loss of nuclear RNA associated with the administration of chemical carcinogens to laboratory test animals on the basis of a nuclear enzyme which has been isolated and purified. This enzyme, an exoribonuclease, preferentially attacks single-stranded, non-helical, rapidly-labeled RNA rather than ribosomal or transfer RNA, which results and produces 5'-mononucleotides. Intact Ehrlich ascites tumor cell nuclei treated with actinomycin D, daunomycin, mithramycin and anthramycin (antibiotics which bind to DNA) did not lose the exoribonuclease activity at concentrations of 2 or 20 μ g/ml; at concentrations of 50 μ g/ml only minimal inhibitory effects on the degradation of endogenous rapidly-labeled RNA was seen in isolated nuclei with actinomycin D, daunomycin and mithramycin. A tentative explanation is proposed that a failure of the proper mechanisms for stabilizing newly-synthesized RNA is caused by agents such as actinomycin D or aflatoxin; such a situation may make newly-synthesized RNA more susceptible to exoribonuclease degradation and to alterations which result in carcinogenesis.

2180 HISTOCHEMICAL DEMONSTRATION OF β -GLUCURONIDASE ACTIVITY IN EXPERIMENTAL INFLAMMATORY

PRODUCED BY CROTON OIL IN RATS. (E.) Feher, J. (U. Med. School, Budapest, Hungary), E. H. Jennin, and I. Rannie. *Brit J Exp Path* 52(1):23-26, 1971.

Rats of both sexes were given s.c. and/or i.m. injections of croton oil (0.01 ml) in the right gluteal region; injected rats were killed 1, 2, 3 or 42 days after treatment, and β -glucuronidase activity was assayed in preparations of rat skin using naphthol AS-BI- β -D-glucosiduronic acid as a substrate. Sites of enzyme activity were characterized by the presence of blue granules. In rats given croton oil treatment, epithelial cells and s.c. tissue cells showed at most slight enzyme activity. In rats given croton oil there was a strong granulocytic infiltration of the tissue; the infiltration was most notable on day 3 when croton oil droplets were seen embedded in fibrin cores and in damaged connective tissue cells together with macrophages, monocytes and fibroblasts. During the first 3 days of the inflammatory reaction produced by croton oil, glycosaminoglycans and glycoproteins increased in tissues of treated rats. In treated rats, β -glucuronidase activity increased progressively following croton oil injection and by 6 wk after treatment, enzyme activity was still high. Granules were found intracellularly, especially in the fibroblasts surrounding droplets of croton oil.

2181 ON THE MECHANISM OF ACTION OF CARCINOGENIC AROMATIC AMINES: II. BINDING OF N-HYDROXY-N-ACETYL-4-AMINOBIPHENYL TO RAT LIVER NUCLEIC ACIDS IN VIVO. (E.) Kriek, E. (Netherlands Cancer Institute, Amsterdam). *Chem Biol Interact* 3(1):19-28, 1971.

Male white rats of the highly inbred R-Amsterdam strain were injected i.p. with N-hydroxy-4-acetylamino- 3 H-biphenyl and N-hydroxy-N-2'- 3 H-acetylamino-biphenyl, and carcinogen-liver nucleic acid binding values were observed 24 hr later. Venom phosphodiesterase and alkaline phosphatase digests of liver were analyzed by Sephadex LH-20 column chromatography. Only 11.7% of the total tritium present in the ethanol eluate of liver extracts cochromatographed with N-(guanosin-8-yl)-4-acetylamino-biphenyl. The level of binding of the amines to DNA was about 10% less than in the case of N-hydroxy-2-acetylamino-fluorine. Twenty percent of the total radioactivity bound to ribosomal RNA appeared in the effluent containing unlabeled N-(guanosin-8-yl)-4-aminobiphenyl as a marker. The remaining eluate, constituting 10% of the radioactivity, was eluted in 3 distinct peaks of unidentified material; the major fraction of radioactivity was associated with R_G values of 2.0 and 2.50.

2182 QUANTITATIVE CHANGES IN THE NUMBER OF INFLAMMATORY CELLS IN EXPERIMENTAL INFLAMMATION PRODUCED BY CROTON OIL IN RATS. (E.) Feher, J. (U. Med. School, Budapest, Hungary), E. H. Jennin, and I. Rannie. *Brit J Exp Path* 52(1):27-30, 1971.

rats were injected with croton oil and killed 4 hr or 1-28 days later, at which time the numbers of mast cells in the vicinity of the croton oil-induced inflammation were observed. Mast cells in s.c. tissue and in the gluteal muscle layer area numbered 1008 and 606 (mean numbers in 2.38 mm^2 field) resp., in rats not treated with croton oil. In croton oil-treated rats mast cells in the s.c. tissue and gluteal muscle numbered 1428 and 588, resp., after 4 hr. By 3 days postinjection, s.c. tissue and muscle cell mast cell numbers were 3244 and 1522, resp. Maximum numbers of mast cells were observed on day 11, at which time the numbers of s.c. tissue and muscle cell mast cells were 770 and 2037, resp. After day 11 the number of mast cells began to decline, and on day 28 s.c. tissue had 6363 mast cells and muscle tissue had 881 mast cells. These results suggest the involvement of mast cells in the croton oil inflammation reaction in the rat.

2183 ACTIVATION OF THE CARCINOGEN, N-HYDROXY-2-FLUORENYLBENZENESULFONAMIDE, BY DESULFON-
YLATION TO N-2-FLUORENYLHYDROXYLAMINE *IN VIVO*. (E.)
Malejka-Giganti, D. (Lab. Cancer Res., VA Hosp.,
Minneapolis, Minn.), H. R. Gutmann, R. E. Rydel and
J. Yost. *Cancer Res* 31(6):778-788, 1971.

Male rats (10-12/group) were administered N-hydroxy-2-fluorenylbzenesulfonamide (NHFBS, 4 mg/100 g) and 2-fluorenylbzenesulfonamide (NFBS, 3.8 mg/100 g) and 2-nitrosofluorene (NF, 2.3 mg/100 g) by stomach tube for 4 months; the dosages of each compound were doubled from 4-6 months and then reduced to initial levels for the last month. Another group of male and female rats received 4.5 mg of compounds/100 g i.p. 3 times/wk for 2 wk. A third group of male and female rats were given the compounds by stomach tube or by i.p. administration to test for the presence and identification of urinary metabolites. NFBS appeared to be relatively nontoxic for the rats; weight gains of the rats receiving the compound were 12% less than controls at the end of 2 months. Similar nontoxicity was noted after i.p. injection. NFBS administration resulted in a tumor incidence of 40-63%; carcinogenicity was more marked following i.p. administration. Metabolites such as N-hydroxy-2-fluorenylacetamide (FAA), 3-, 5-, or 7-hydroxy-FAA were isolated from the urine of animals treated with NFBS; the N-hydroxy-2-FAA accounted for 70% of the isolated urinary metabolites. N-Phenyl-2-fluorenylhydroxylamine was found to have weak carcinogenic properties, probably because the molecule cannot be cleaved, as can the N-acylarylhydroxylamines, to form the proximate carcinogen, N-2-fluorenylhydroxylamine.

2184 INDUCTION OF MALIGNANT TUMORS IN RATS BY
ORAL ADMINISTRATION OF 2-IMIDAZOLIDINONE
AND NITRITE. (Ger.) Sander, J. (Hygiene Inst.,
Tübingen, Germany) and G. Bürkle. *Z Krebsforsch*
5(4):301-304, 1971.

Two groups of SIV 50 female rats (6 each) were maintained on a standard diet to which 0.1% 2-

imidazolidinone was added; in addition, group II received 0.12% of sodium nitrite in their drinking water. Food and water were given *ad lib* and the treatment lasted for 150 days. Five of the 6 rats receiving nitrite developed kidney tumors with histological features corresponding to human nephroblastoma. One animal developed lung metastases and another rat developed in addition a papillomatous mammary gland adenoma; the rat with no kidney tumor developed a keratinizing squamous cell carcinoma in the parotid region. No tumors were observed in the group that did not get nitrite; all rats in this group survived to the end of the experimental period (when the last rat of group II died) and were then sacrificed 311 days after the beginning of the experiment. The induction of malignant tumors by oral administration of 2-imidazolidinone and nitrite indicated that the amide group is easily converted into the corresponding carcinogenic nitrosoderivative *in vivo*.

2185 ANIMAL EXPERIMENTS ON THE CARCINOGENIC ACTION OF METHOTREXATE AND CYCLOPHOSPHAMIDE.
(Ger.) Roschlau, G. (Med. Acad. Carl Gustav Carus, Dresden, Germany) and J. Justus. *Deutch Gesundh* 26(5):219-222, 1971.

Biweekly injections (i.p., 25 mg/kg x 30, total dose of 750 mg) of cyclophosphamide and 55 mg (0.1 mg/kg/day, p.o. drinking water) of methotrexate were administered to male and female XVII/B1n and AWD mice. Both agents at these therapeutic dose levels showed definite carcinogenic effects in 18-24 months in all groups, with lung adenoma and carcinoma predominantly present and, to a lesser degree, hepatoma and skin carcinoma and sarcoma. The rate of lung tumor induction was markedly above that of spontaneous tumor formation, with methotrexate treatment showing particularly high incidence. Pregnancy often disposed towards a higher incidence of malignancy in cyclophosphamide-treated animals (an observation of significance in human oncology) and untreated offspring of mothers treated with cyclophosphamide during pregnancy showed increased rate of tumor formation, suggesting transplacental oncogenetic drug action.

2186 PANCREATIC ISLET CELL TUMORS PRODUCED BY
THE COMBINED ACTION OF STREPTOZOTOCIN AND
NICOTINAMIDE. (E.) Rakieten, N. (South Shore
Analytical and Res. Lab., Inc., Islip, N.Y.), B. S.
Gordon, A. Beaty, D. A. Cooney, R. D. Davis and
P. S. Schein. *Proc Soc Exp Biol Med* 137(1):280-283, 1971.

Male rats were given streptozotocin and/or nicotinamide according to 1 of 3 protocols: a single i.v. injection of 50 mg/kg streptozotocin together with 2 i.p. injections of 350 mg/kg nicotinamide; 50 mg/kg streptozotocin alone; or 350 mg/kg nicotinamide alone. Controls were given an 0.025 M solution of citric acid in saline. Pancreatic islet cell tumors developed in 64% of the rats given both streptozotocin and nicotinamide; tumors first ap-

peared 226 days after treatment, and 83% of tumors had developed by days 438-547. Only 1 islet cell tumor developed in rats given streptozotocin alone, and no islet cell tumors developed in either nicotinamide-treated rats or in controls. Tumors appeared to be reddish brown bodies weighing 50-70 mg and were insulin-secreting; they were first seen in the tail of the pancreas adjacent to the hilus of the spleen. The tumor cells had centrally placed nuclei which lacked nucleoli.

- 2187 CARCINOGENIC ACTION OF DIMETHYLSULFOXIDE (DMSO). (Ger.) Lohs, Kh. (Inst. Chem. Toxicol. D.A.W., Berlin-Buch, Germany), W. Damerau and T. Schramm. *Arch Geschwulstforsch* 37(1):1-3, 1971.

Young Wistar rats (8 wk), injected s.c. 10 times biweekly with either or both $TiCl_3$ + DMSO + H_2O and H_2O_2 + DMSO + H_2O showed no signs of tumor formation over the subsequent year. This is contrary to the view that methyl and methane sulfonyl radicals found in the reaction of DMSO and H_2O_2 in the presence of heavy metal ions may have carcinogenic effects.

- 2188 IMMUNOSUPPRESSIVE ACTIVITY OF THE ONCOGENIC PURINE DERIVATIVE 3-HYDROXYXANTHINE. (E.) Teller, M. N. (Sloan-Kettering Inst. Cancer Res., New York, N.Y.) and I. Smullyan. *Israel J Med Sci* 7(1):66-71, 1971.

Young male rats were injected with 1 of 4 carcinogens and the degree of immunosuppression induced by the agents was observed; the carcinogens included 3-hydroxyxanthine (1 or 7 mg), 3-methylcholanthrene (1 or 6 mg), cortisone (20 mg) and cyclophosphamide (2.6 mg). To test the effects of carcinogens on the hemagglutinin antibody response, rats were given injections of antigenic sheep red blood cells following carcinogen administration. Saline-treated rats showed (\log_2) antibody titers of 12.0 to sheep red blood cells compared to 3-hydroxyxanthine-treated rats which showed titers of 5-9. Methylcholanthrene and cortisone inhibited the antibody response to a similar degree as 3-hydroxyxanthine; cyclophosphamide almost entirely suppressed the antibody response (titers of 0.6). The effect of carcinogens on homograft response was studied in rats implanted with sarcoma tissue. In untreated rats and in rats treated with saline, tumors developed in 30 and 0% of cases, resp. In rats given 7 mg of 3-hydroxyxanthine, tumors developed in 50% of cases, and in rats given 1 mg of this agent the tumor incidence was 20%. In rats given methylcholanthrene in addition to 3-hydroxyxanthine the tumor incidence was 40%, and in rats given 8 mg of cortisone in addition to carcinogen the tumor incidence was 100%. Cortisone enhanced the effect of 3-hydroxyxanthine.

- 2189 MORPHOLOGICAL ALTERATIONS OF THE ANIMAL SKIN FOLLOWING SINGLE APPLICATION OF CARCINOGENIC HYDROCARBONS. (Rus.) Vasil'yeva,

N. H. (Inst. Exp. Clin. Oncol. Acad. Med. Sci. U.S.S.R., Moscow). *Biull Eksp Biol Med* 71(3):116-119, 1971.

The morphology of the skin reaction to a single application of 7,12-dimethylbenz(a)anthracene (DMBA), 3-methylcholanthrene (MC) benzo(a)pyrene (BP), pyrene (P) or anthracene (A) was investigated in 287/A and C57BL randombred mice and in Wistar and guinea pigs. Benzene solutions of the test hydrocarbons (1% BP or P, 0.5% MC or A or 0.25-0.5% DMBA soln) were applied topically on the intercostal region; the mice were given 2 drops and the rats and guinea pigs were given 5 drops of a test compound soln. The most explicit hyperplastic alterations of the epidermis, in order of intensity, were induced by DMBA, MC and BP and correlated with the carcinogenicity of these compounds. The most intense reactions occurred in mouse skin; a severe decrease in sebaceous glands 3-5 days after carcinogen treatment along with hyperplastic alterations of the epidermis were observed; the sebaceous glands were intact during the whole experimental treatment when exposed to P or A. BP-induced dystrophic changes in the sebaceous gland cells occurred on the 1st day after its application. DMBA induced the first signs of atypia and epithelial polymorphism in 9 days and focal proliferation in 11 days following application. Regeneration of the sebaceous glands after MC or BP treatment was observed 7-9 days after 15-17 days, resp., after DMBA application. The premalignant transformations of the epidermis were usually correlated with specific alterations of connective tissue. Fluorescence studies of fresh frozen mouse skin sections revealed the longest retention time within the sebaceous glands for BP (up to 7 days); BP retention time was 3 days for MC and 1 day for DMBA.

- 2190 PYRROLE PIGMENTS OF ORGANS IN 2-AMINO-FLUORENE-INDUCED CARCINOGENESIS IN RATS. (Ger.) Zawirska, B. (Inst. Pathol. Anat. Acad. Med. Sci., Wroclaw, Poland), K. Medras and Sosnik. *Zbl Allg Path* 114(1):41-50, 1971.

The chronic feeding of 2-acetylaminofluorene (2-AAF) (2 mg daily for 3-14 months) induced epithelial tumors in various organs, but particularly in the liver, of Wistar rats. The transplanted liver carcinomas produced pulmonary metastases. Macrofluoroscopic examination of the tissues and organs and the liver cell carcinomas showed no porphyrin fluorescence except in the Harderian glands, which fluoresced red. Microfluoroscopic examination of livers at different stages of the 2-AAF feeding and of the transplanted liver cell carcinomas were all negative for red fluorescence. Biochemical determinations of uroporphyrin, coproporphyrin and protoporphyrin performed between 75-380 days from the beginning of the experiment showed similar values in experimental and control animals; the highest porphyrin values were found in Harderian glands. The concentration of uroporphyrin/g of tissue was higher of the porphyrins in all organs. During porphyrin extraction from tissues, particularly from liver cell carcinomas, a greenish substance was observed.

ich resembled bile pigments but behaved to a certain extent like porphyrin. It is suggested that this substance is derived from the splitting of the pyrrole ring.

91 INHIBITION OF PITUITARY-INDUCED NODULAR HYPERPLASIA IN MAMMARY GLANDS OF C3H MICE FED A PHENYLALANINE-DEFICIENT DIET. (E.) Forni, A. ("Luigi Devoto" Work Clin., U. Milan, Italy), E. Pacifico and A. Limonta. *Arch Environ Health* 22(3):373-378, 1971.

male virgin mice of strain C3H/Crgl were maintained for 19 wk on diets containing phenylalanine w/w levels ranging from 0.075-0.300%; mammary glands of mice were stimulated by a pituitary iso-raft implanted under the kidney capsule for the first 13 wk of phenylalanine feeding. Phenylalanine deficiency in the diet was found to increase the development of mammary hyperplastic nodules. Mice given 0.075-0.090% phenylalanine developed no nodules; 0-16% of mice given 0.120% phenylalanine developed nodules; 50-100% of mice given 0.150-0.300% phenylalanine developed nodules. High levels of dietary phenylalanine increased the body wt of mice. The ratio of organ wt to body wt for ovaries, but not liver, kidneys or adrenals, was lower for mice fed with 0.075-0.120% phenylalanine. Ovaries of mice in this experimental group lacked corpora lutea.

92 MOLECULAR SPECIFICITY OF THE TUMORIGENIC ACTION OF ETHIONINE: THE INACTIVITY OF S-ETHYL-L-CYSTEINE: ACTION ON RESPIRATORY PARAMETERS. (E.) Argus, M. F. (Dept. Med., Tulane U., New Orleans, La.), L. E. White, G. M. Bryant, J. C. Hoskins and C. Hoch-Ligeti. *Z Krebsforsch* 73(3):201-208, 1971.

The structure-effect relationship of the ethionine molecule was investigated. Oncogenicity of ethionine was compared to that of S-ethyl-L-cysteine (SELC) and their effects on the phosphorylation processes in rat liver mitochondria using α -ketoglutarate, hydroxybutyrate or succinate as substrates were investigated. Male Wistar rats received a total of 6 g of SELC p.o. within 90 wk or a total of 6 g of ethionine p.o. within 52 wk. SELC appeared to be non-oncogenic while ethionine produced a 100% incidence of liver tumors. Ethionine produced a decrease both the P/O ratio and the respiratory control index (RCI) *in vivo* in female but not in male rats. The P/O ratio decreased in female rat mitochondria upon ethionine treatment *in vitro*. SELC had no effect on the P/O ratio when assayed with either of the above-mentioned substrates. No alterations in the QO_2 were observed to be produced by ethionine or SELC. The increased availability of ATP, through "trapping" of adenosyl moieties by ethionine, seemed to be masked by other alterations in ATP biosynthesis. The effects of ethionine on the phosphorylation processes seemed to be related to its fatty liver inducing properties in female rats rather than to its

carcinogenicity. The lack of oncogenic effects elicited by SELC seemed to indicate the necessity of the 4 carbon chain structure in the ethionine molecule.

2193 CHROMOSOME STUDIES IN WORKERS EXPOSED TO BENZENE OR TOLUENE OR BOTH. (E.) Forni, A. ("Luigi Devoto" Work Clin., U. Milan, Italy), E. Pacifico and A. Limonta. *Arch Environ Health* 22(3):373-378, 1971.

Peripheral blood lymphocytes from 34 workers in a rotogravure printing plant were examined for chromosomal aberrations; 10 of the workers had been exposed to benzene and/or toluene in the course of their work, and 24 of the workers had been exposed to toluene only. Duration of exposure to benzene and toluene ranged from less than 1 yr to 22 yr, while duration of exposure to benzene alone (2 cases) was 2-3 yr and duration of exposure to toluene alone ranged from 3-15 yr. Subjects ranged in age from 29-58-yr-old. The incidence of unstable chromosome changes was higher in the group exposed to benzene than in the group exposed to toluene (incidences of 1.66% and 0.80%, resp.); however, the incidence of unstable chromosome changes in the toluene group was not significantly different from that in a group of matched controls not exposed to either benzene or toluene (0.61% incidence in controls). The incidence of calculated breaks in chromosomes undergoing unstable changes was also higher in the benzene group than in the toluene group or in controls; the percentages of calculated breaks in the benzene group, the toluene group and the controls were 1.87, 0.83 and 0.67%, resp.

2194 STIMULATORY EFFECTS OF CHEMICAL CARCINOGENS IN CELL CULTURES. (Rus.) Parkhomenko, I. I. (Inst. Chem. Phys., Acad. Med. Sci., U.S.S.R., Moscow) and I. S. Irlin. *Vop Onkol* 17(3):81-85, 1971.

Small doses of the chemical carcinogens, benzo(a)-pyrene, (0.02, 0.1, 1 mg/ml) and 7,12-dimethylbenz(a)anthracene (DMBA 0.01, and 0.1 mg/ml) had a stimulatory effect on the *in vitro* growth of hamster cells transformed by polyoma virus strain 874, but these same doses produced an inhibitory effect on the cell growth of normal hamster cells and in cultures infected with the 866 and 610 polyoma virus strain; 3-methylcholanthrene (MC) (0.2 and 1 mg/ml) manifested stimulatory effects on the 874 and also on the 866 polyoma virus-infected cells and was the least toxic of the carcinogens; when tested at doses of 0.2, 1 and 5 mg/ml, MC decreased the *in vitro* growth of the 610 strain. In general, low doses of the carcinogens had a stimulatory effect, while doses as high as 5 mg/ml had an inhibitory effect on *in vitro* culture growth. The noncarcinogenic analogs, purine and anthracene, were less toxic and were most effective stimulants of the 874 cell line at a dose of 0.1 mg/ml. The simultaneous addition of 2 carcinogens at the doses of 0.1 for DMBA and 1.0 mg/ml for MC also proved to be growth stimulating. A stimulatory dose of anthra-

cene (1.0 mg/ml) could not alleviate the toxic effects of DMBA at 1.0 mg/ml, when the 2 compounds were used simultaneously.

- 2195 THE HAMSTER AS A MODEL FOR METAL CARCINOGENESIS. (E.) Furst, A. (Inst. Chem. Biol., U. San Francisco, Calif.) and M. C. Schlauder. *Proc West Pharmacol Soc* 14(68):68-71, 1971.

Syrian hamsters of both sexes after 3-4 wk were given i.m. injections of pure metal and organometallic compounds once a month. The compounds tested included nickel powder, nickelocene, and titanocene dichloride. The incidence of tumors developing in treated hamsters was not high and ranged from 0 tumors in 50 hamsters given 5 mg nickelocene to 4 tumors in 29 hamsters given 25 mg nickelocene. Metallic compounds produced a much higher tumor incidence (36-76%) when administered to rats. Tumor-like nodules appeared with 3 months from the start of metal treatments in hamsters and regressed over time; rats did not develop nodules until 7-10 months after the start of the carcinogenic regimen. In hamsters receiving transplants of tumors induced by the metal carcinogens, a 100% tumor-take was seen. Tumors induced in hamsters by the metals were poorly differentiated fibrosarcomas composed of spindle-shaped cells and rich in collagen. The presence in hamster tumors of aggregations of plasma cells and lymphocytes suggested a host immune response to the metal carcinogens which was not observed in the rat.

- 2196 THE ROLE OF OVERHEATED FOOD FATS IN CARCINOGENESIS. (Rus.) Turkiya, N. B. (Sci. Res. Inst. Oncol. Min. Pub. Hlth. Georgian S.S.R., Tiflis, U.S.S.R.), G. L. Chechelashvili, P. N. Krasnyanskaya, D. Sh. Beniashvili and L. N. Dzagnidze. *Vop Pitan* 1:31-34, 1971.

The carcinogenicity of butter and sunflower oil heated to 160-180°C for 30-40 min was tested by p.o. and i.m. treatment of 260 randombred rats. P.O. treatment of 100 rats consisted of 3 ml of heated oil or butter alone on alternate days for 1.5 yr or combined with 3 doses of 2 mg of benzo(a)pyrene (BP) given at 1 wk intervals at the beginning of the experiment. The i.m. treatment (160 rats) consisted of 6 injections of natural or heated butter or oil (2 ml at 10-day intervals) alone or combined with a single dose of 1 mg of BP dissolved in benzene. No tumors occurred in the p.o.-treated rats; 19 of 116 i.m.-treated rats developed tumors 4 months after the beginning of the experiment. The highest incidence of tumors (5 out of 10 rats) was noticed among the animals exposed to heated butter associated with BP and no tumors occurred in the rats treated with unheated fats. The development of tumors could be attributed to the formation of thermoresistant oxidation products during the heating of the tested fats.

- 2197 IN VITRO TRANSFORMATION OF HAMSTER CELLS BY POLYCYCLIC HYDROCARBONS: FACTORS INFLUENCING THE NUMBER OF CELLS TRANSFORMED. (E) DiPaolo, J. A. (Natl. Cancer Inst., Natl. Inst. Bethesda, Md.), P. J. Donovan and R. L. Nelson. *Nature* 230(16):240-242, 1971.

Primary, secondary or tertiary Syrian hamster cells 2-4 days old were exposed to benzo(a)pyrene (2.5 µg/ml) or balanced salt solution and diluted with complete medium one day after the hamster embryo cells had been seeded with irradiated rat cells feeders. Under stereoscopic microscopy primary secondary cultures exhibited a wide variety of different types of colonies, and a proportional decrease in variety was noted with increased concentration of the carcinogen. Twelve different cell morphologies were recognized among fibroblast-like and epithelial-like transformations; organ cells revealed less variety. The seeding of 500 cells provided for transformation/cell percentage ranging from 0.2 to 0.73%; the cloning efficiency of the different cultures in the presence of carcinogen varied from low of 3% to a high of 5.9% which occurred when feeders were added 48 hr before the addition of hamster cells and lowest when the feeders were added subsequent to the hamster cells. Transformation was influenced by the number of feeders used; 2 irradiated rat cells had a relatively poor feeding effect in contrast to 50-100,000 cells which produced optimal effects. However, the addition of a million feeder cells practically suppressed the recognition of transformed colonies.

- 2198 PROPERTIES OF CHROMATIN FROM LIVER AND FROM A CHEMICALLY INDUCED MINIMAL DEVIATION HEPATOMA OF THE RAT. (E.) Smith, C. E. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), P. T. Mora. *Biochim Biophys Acta* 232(4):643-651, 1971.

A minimal deviation hepatoma carried by i.m. transplantation in female Buffalo strain rats revealed its DNA and chromatin UV spectra and the thermal denaturation profiles of its chromatin to be nearly identical to their liver counterparts. Higher content of RNA (RNA/DNA=0.38) was associated with the hepatoma chromatin than in liver chromatin (RNA/DNA=0.15). The nucleotide compositions of *in vitro* transcribed RNA products catalyzed by *E. coli* or *M. luteus* polymerase using DNA templates from hepatoma and liver chromatin were similar to each other. All RNA products had a high A+U/G+C ratio of 1.1-1.3. The kinetics of ¹⁴C-CMP incorporation (which increased for at least 40 min at 37°C) and the divalent ion requirements (4mM Mg²⁺, 1 mM Mn²⁺) of DNA-directed *E. coli* RNA polymerase with hepatoma chromatin template appeared to be similar to those known for liver chromatin.

- 2199 CHEMICAL CARCINOGENS AND RNA. (E.) Weinstein, I. B. (Inst. Cancer Res. Dept. Med., Columbia U., New York, N.Y.), D. Grunberger, S. Fujimura and L. M. Fink. *Cancer Res* 31(5):651-655, 1971.

highly purified preparation of *Escherichia coli* tRNA^{fMet} was modified to a low extent by reaction with 1.25×10^{-3} M ^{14}C -N-acetoxy-2-acetylaminofluorene (NAAAF) for 90 min, and the unreacted and AAF-modified tRNA^{fMet} were separated on a BD-cellulose column. The modified tRNA^{fMet} (AAF-tRNA^{fMet}, 5% yield) displayed considerable absorption at 260 nm and melted at a lower temperature and had a lower total hyperchromicity than the control material. Size T₁ treatment and DEAE-Sephadex A-25 column chromatography of AAF-tRNA^{fMet} resulted in the isolation of mainly AAF-modified guanosine. Treatment with pancreatic RNase and chromatography on BD-cellulose DEAE-Sephadex A-25 yielded an AAF-labeled oligonucleotide which seemed to be a G-G-pyrimidine segment. Use of models and analysis of residues showed that AAF becomes covalently linked to position 8 of guanosine residues. This attachment may distort the formation of the tRNA, thereby altering interactions with aminoacyl-tRNA synthetases, codons, and/or ribosomes, resulting in widespread disturbances of the translation apparatus, with secondary consequences with respect to cell differentiation, regulation and autonomy.

ONCOGENIC RESPONSE OF RAT SKIN, LUNGS, AND BONES TO VINYL CHLORIDE. (E.) Viola, L. (Regina Elena Inst. Cancer Res., Rome, Italy), Bigotti and A. Caputo. *Cancer Res* 31(5):516-522, 1971.

The rats were exposed to vinyl chloride vapors for 5 hr per day, 5 days per wk for 12 months; the vinyl chloride was diffused into the air of the containers which held the rats in amounts of 3% vinyl chloride (30,000 ppm). Almost all the rats developed tumors of the skin and lungs. Among 17 rats surviving the 12 month course, all had skin tumors and 6 had lung tumors; 5 of the 17 had bone tumors. Most of the tumors were epidermoid carcinomas; there were also epidermoid carcinomas and 2 epidermoid carcinomas of the keratinizing type. Among lung tumors, there were 3 adenocarcinomas, a squamous cell carcinoma and an adenocarcinoma. Bone tumors were localized in the metacarpal and metatarsal bones of 4 extremities; all were osteochondromas. Skin tumors were localized in the area of the submaxillary and parotid glands.

QUANTITATIVE CHANGES IN UNSCHEDULED DNA SYNTHESIS IN RAT MUSCLE CELLS AFTER DIFFERENTIATION. (E.) Hahn, G. M. (Stanford U. Sch., California), D. King and S.-J. Yang. *Nature* 231(526):242-244, 1971.

Uninucleated rat muscle cells and fibroblasts obtained from rat embryos on the nineteenth day of gestation were exposed to methyl methane sulfonate (MMS) for 7 hr followed by labeling with ^3H -thymidine for 3 hr. Exposure for 3 hr to 1 mM MMS reduced the number of cells with more than 100 grains, indicating inhibition of normal DNA synthesis. However, the number of unlabeled cells was also greatly reduced and unscheduled DNA synthesis. Nuclei from myo-

tubes revealed almost no label even after exposure to MMS; however if the time of exposure was greatly increased, unscheduled DNA synthesis could be detected.

2202 POLYCYCLIC AROMATIC HYDROCARBONS IN SMOKED FISH, "KATSUBUSHI". (E.) Masuda, Y. (Fac. Med., Kyushu U., Japan) and M. Kuratsune. *Gann* 62(1):27-30, 1971.

Chromatography on alumina columns and on partially acetylated paper and UV absorption spectroscopy were used to determine the content of polycyclic aromatic hydrocarbons in the smoked and dried fish dishes Katsubushi, Sababushi, and Urumbushi. These dishes are prepared by smoking the flesh of bonito, mackerel and sardine over wood fires for periods of about 1 wk. Polycyclic aromatic hydrocarbons detected in the fish included phenanthrene, pyrene, fluoranthrene, benz(a)anthracene and benzo(a)pyrene. Katsubushi generally contained more hydrocarbons than the other dishes. The amounts of benzo(a)pyrene found in Katsubushi, Sababushi and Urumbushi were 37, 12 and 2 $\mu\text{g/kg}$, resp. It was found that these Japanese smoked fish contained significantly higher concentrations of polycyclic aromatic hydrocarbons than smoked fish from other countries.

2203 CYTOGENETIC EFFECTS OF CYCLOHEXYLAMINE AND N-OH-CYCLOHEXYLAMINE ON HUMAN LEUCOCYTES AND CHINESE HAMSTER BONE MARROW. (E.) Brewen, J. G. (Oak Ridge Nat. Lab., Tenn.), F. G. Pearson, K. P. Jones and H. E. Luippold. *Nature* 230(9):15-16, 1971.

Short term human leukocyte cultures were exposed to 20, 100, or 500 $\mu\text{g/ml}$ of cyclohexylamine (CHA) at the G₀, G₁, S, or G₂ phase of the mitotic cycle; leukocytes were also exposed to 25, 50, 100, 200, or 250 $\mu\text{g/ml}$ of N-hydroxycyclohexylamine (N-OHCHA) in all mitotic stages except the G₀ phase. In related *in vivo* experiments, hamsters were given implanted diffusion chambers containing human leukocytes and treated with CHA. The hamsters were killed 60-66 hr after implantation and the diffusion chambers were withdrawn for examination. In none of the experiments was there an increase in the incidence of chromatid breaks occurring in CHA-treated or N-OHCHA-treated leukocytes. Asymmetric chromosome exchanges (including rings and dicentric) were seen to have a very low frequency in treated and in untreated leukocytes.

2204 COCARCINOGENESIS STUDIES ON MOUSE SKIN AND INHIBITION OF TUMOR INDUCTION. (E.) Van Duuren, B. L. (New York U. Med. Ctr., New York), T. Blazej, B. M. Goldschmidt, C. Katz, S. Melchionne and A. Sivak. *J Nat Cancer Inst* 46(5):1039-1044, 1971.

Female strain ICR/Ha Swiss mice were given topical applications of linalyl oleate and linalyl acetate

together with benzo(a)pyrene (1 or 5 μ g 3 times/wk) to test the co-carcinogenic effects of tobacco leaf and smoke derivatives. Other derivatives including phenol, solanesol, rutin, morin and linalyl laurate were also tested. Linalyl oleate and linalyl acetate showed slight co-carcinogenic activity, while phorbol myristate acetate was strongly co-carcinogenic. Linalyl acetate, bornyl acetate, bornyl laurate and bornyl oleate showed no co-carcinogenic activity. Phenol, rutin and morin produced decreased tumor yield by comparison to the yield produced by benzo(a)pyrene alone.

- 2205 THE EFFECT OF AFLATOXIN B₁ ON RNA SYNTHESIS AND BREAKDOWN IN NORMAL AND REGENERATING RAT LIVER. (E.) Wagner, L. (Med. Clin., U. Heidelberg, Germany) and J. Drews. *Europ J Cancer* 6(6):465-476, 1970.

Partially hepatectomized rats were given i.p. injections of 1.0-1.25 mg/kg of body wt aflatoxin B₁, and the ensuing changes in the metabolism of nuclear RNA in the regenerating liver were observed. A 30-50% decline in the incorporation of labeled RNA precursors to liver RNA was seen within 2.5 hr after aflatoxin treatment. Aflatoxin was found to hinder the formation of the 35S ribosomal precursor RNA and of 28S RNA. A change to more DNA-like values was seen in the ³²P-nucleotide composition of total nuclear RNA extracted after pulse-labeling with ³²P-ortho-phosphate. A rise in the AMP + UMP/CMP + GMP ratio of the ³²P-labeled RNA followed aflatoxin treatment; this rise was more marked in regenerating liver than in normal liver from intact rats. *In vitro* experiments demonstrated that nuclei from aflatoxin-treated rats had less capacity to synthesize RNA than did nuclei from untreated rats.

- 2206 THE INFLUENCE OF POSTNECROTIC CIRRHOSIS ON AFLATOXIN CARCINOGENESIS IN RATS. (E.) Sun, S.-C. (United States Naval Med. Res. Unit No. 2, Taipei, Taiwan), R.-D. Wei and B. T. Schaeffer. *Lab Invest* 24(5):368-372, 1971.

Crude aflatoxin preparations containing 57% B₁, 41% G₁ and trace amounts of B₂ and G₂ dissolved in N,N-dimethylformamide-propylene glycol (1 mg/ml) were administered to 4 experimental groups of rats 4-6 wk following CCl₄ and/or ethanol pretreatment. Rats with moderate to severe CCl₄-induced postnecrotic cirrhosis given 200 μ g/wk of toxins (i.p. for 3 wk) developed hepatoma in 11 of 16 cases and advanced liver cell atypia in 5 of 16 cases within 12 wk; rats with ethanol-induced fatty liver developed no tumors under similar experimental conditions. When treated for 8 wk with similar weekly amounts of toxin 13 of 20 rats died within 37 wk (3 with hepatocarcinoma); of the 7 surviving rats 2 developed liver cell cancer, 3 had advanced hepatocellular atypia, and 2 had atypical canalicular hyperplasia. Postnecrotic cirrhosis seemed to promote aflatoxin-induced hepatocarcinogenesis with early malignant transformations occurring within the cirrhotic nodules.

- 2207 AFLATOXIN B₁: THE KIDNEY AS A SITE OF ACTION IN THE MOUSE. (E.) Akao, M. (Dept. of Nutrition and Food Science, Massachusetts Inst. Tech., Cambridge), K. Kuroda and G. N. Wogan. *Lipid Sci* 10(9):495-501, 1971.

Aflatoxin B₁ was injected i.p. to 100-120 day-old CFW Swiss mice at 60 mg/kg, single dose. ¹⁴C-Orotic acid (22.6 C/mole) was injected at a dose of 25 μ mol, 1, 12, 24 or 72 hr after toxin injection. Three days later, the mice were killed and incorporation of precursor into RNA of liver and kidney tissues was determined. A 50% suppression of precursor incorporation was evident in the kidney within 3 hr after toxin administration and persisted through the 72 hr period of study. The RNA content of kidneys decreased rapidly to less than 50% of control values and pronounced hemorrhagic lesions developed in the medullary portions between 48 and 72 hr. No similar alteration in either precursor uptake or histology was seen in the liver. RNA polymerase activity decreased from 258 to 138 p moles UTP/mg DNA under Mg²⁺ activation and from 652 to 454 p moles UTP/mg DNA under Mn²⁺ activation in the kidney of toxin-treated mice. No inhibition of RNA polymerase under either condition of activation was apparent in liver nuclei isolated from aflatoxin-treated mice. The responses occurring in kidneys but not in the liver of mice may be due to the presence in mouse kidney of chromatin with sites of interaction for the toxin which are not present in the liver.

- 2208 INDUCTION OF RECESSIVE LETHALS IN *Drosophila melanogaster* BY AFLATOXIN B₁. (E.) Lamb, M. J. (Zool. Dept., Birkbeck Coll., London, England) and L. J. Lilly. *Mutat Res* 11(4):430-433, 1971.

Male *Drosophila melanogaster* were given p.o. dose of 0.02 mg aflatoxin B₁ in a 0.5% dilution of DMSO administered to females; the incidence of 11nd chromosome recessive lethals was observed in the offspring of the aflatoxin-treated *Drosophila*. The percentage of lethals found in the offspring of 100 *Drosophila* fed DMSO ranged from 0-0.69 \pm 0.34%, while the incidence of lethals among offspring of *Drosophila* given aflatoxin B₁ ranged from 0.53 \pm 0.30 to 3.66 \pm 0.30.

- 2209 ACUTE TOXICITY OF AFLATOXIN G₁ TO THE RAT. (E.) Butler, W. H. (Med. Res. Council, Carshalton, Surrey, England) and W. Lijinsky. *J Path* 102(4):209-212, 1971.

Male rats were treated with aflatoxin G₁ (0.15-0.30 mg/ml) either by i.p. injection or by gavage, and the ensuing lesions were described. Diffuse parenchymal cell necrosis, especially prominent in the periportal zone, was seen in the livers of rats 2-7 days after treatment. After 7 days, the major change seen in liver parenchymal cells was that nuclei became enlarged and hyperchromatic. By 2 days after treatment proliferation in bile duct epithelium was seen; proliferation became maximal at 6-7 days after treatment. In more severely affected

ated rats, hyperplastic nodules and areas of angiofibrosis were present. By 1-2 days after treatment the epithelium of the straight segments of the proximal tubules of the kidney showed eosinophilic cytoplasm; at 3-4 days the kidney tubules showed necrosis. By 3-4 wk after treatment, the only abnormality seen in the kidneys of treated rats was the presence of many large hyperplastic epithelial cells. The adrenals of treated rats showed extensive hemorrhagic necrosis involving the zona reticularis by 2-3 days after treatment. Other organs affected by aflatoxin G₁-treated rats included the lungs and para-aortic lymph nodes. Aflatoxin G₁ did not produce liver lesions as did aflatoxin B₁.

ABSENCE OF AN EFFECT OF PARTIAL HEPATECTOMY ON AFLATOXIN B₁ CARCINOGENESIS. (E.)

ers, A. E. (Dept. Nutrition Food Science, Massachusetts Inst. Tech., Cambridge), N. S. Kula and P. Newberne. *Cancer Res* 31(5):491-495, 1971.

Fischer and Sprague-Dawley strain rats were given 375 µg aflatoxin B₁ (AFB) immediately, 24 hr, 48 hr, 6 days or 1 wk after partial hepatectomy; in 1 wk group, AFB was given prior to hepatectomy. Hepatectomy performed before or after AFB administration did not affect the incidence of hepatomas developed in treated rats compared to that in rats given AFB without hepatectomy. However, when AFB treatment was given 6 hr after either hepatectomy or sham operation the incidence of liver carcinomas was less than in rats given AFB beginning 24 hr or 6 days after hepatectomy or sham operation. Fischer rats seemed to be more sensitive to AFB carcinogenesis than were Sprague-Dawley rats.

THE CHANGING PATTERN OF CARCINOGENIC AMINOAZO DYE-BINDING PROTEINS DURING THE COURSE OF CONTINUOUS FEEDING OF 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE. (E.) Sugimoto, T. (Fac. Science, U. Tokyo, Japan) and H. Terayama. *Chem-Biol Interact* 2(4):391-400, 1970.

Wistar rats fed a semisynthetic diet containing 0.06% 3'-methyl-4-dimethylaminoazobenzene and *ad lib* were sacrificed at 2 wk, 1, 3 or 10 weeks, and the livers were homogenized to provide liver sap for protein-bound dye and arginase assay. Protein content of the cell sap ranged from 15.7-27.1 mg/g liver; protein-bound dye range from 1.5-15.4 nmoles/g liver. The arginase content ranged from 164-346 U/g liver in azo dye fed animals compared to 5 control rats with 143 U/g and 3 hepatoma-bearing rats with 29 U/g. Throughout the study, the protein-bound dye as well as the arginase activity present in the liver cell sap was recovered almost completely in response to heat-treatment; the enzyme activity in livers of rats on continuous azo dye feeding proved to be rather labile, compared with activity noted in previous experiments with single doses, and was ultimately lost with subsequent chromatographic separation. As dye feeding progressed an increasingly retarded elution pattern

for basic protein fractions which was associated with more and more dye-binding was seen. Binding to the nonbasic proteins tended to decrease soon after the onset of dye-feeding.

2212 DNA OF RAT HEPATOMAS: SEARCH FOR GENE AMPLIFICATION. (E.) Shearer, R. W. (Dept. of Pathology, U. Wash., Seattle). *Biochem Biophys Res Commun* 43(6):1324-1328, 1971.

Differences between the DNAs of primary and transplantable rat hepatomas and normal rat liver kidney and lung tissues were investigated. Primary hepatomas DB-2E, DS-10B and DS-11D were induced in male rats by chronic feeding with a low riboflavin diet containing 0.06% 3'-methyl-dimethylaminoazobenzene. DB-2E grew in a Buffalo rat, while DS-10B and DS-11D grew in Sprague-Dawley rats. Tumor FS-1a was induced in the liver of a male Sprague-Dawley rat by chronic feeding of a normal diet plus 0.03% N-2-fluorenylacetamide. Isotope labeling of tumor cell RNA was done in cell culture (³H-uridine 20 µc/10⁶ cells added to the medium for 1 hr). No differences were detected in the rate or degree of annealing or in the shape of the melting curves of the hybrid molecules formed between hepatoma and normal DNAs; thus specific gene amplification was not characteristic for these tumors.

2213 BILE ACID INVOLVEMENT IN AZO DYE CARCINOGENESIS. (E.) Holland, J. C. (Dept. Biol. Sciences, Michigan Tech. U., Houghton) and J. D. Spain. *Cancer Res* 31(5):538-541, 1971.

Male rats were maintained on a diet containing 0.06% 3'-methyl-4-dimethylaminoazobenzene (3'MeDAB) for periods of 66 days; gas chromatography was used to identify bile acids in feces and urine. The feces of azo-dye-fed rats contained 7 bile acids, including lithocholic acid, deoxycholic acid, cholic acid and hyodeoxycholic acid. Deoxycholic acid was the prominent acid in the feces of rats on the carcinogenic diet. Of 112 rats given a normal diet, only 2 showed measurable quantities of bile acids; however, the urine of dye-fed rats showed significant amounts of cholic acid, hyodeoxycholic acid and ursodeoxycholic acid, these acids showing elevated assays in the urine of carcinogen-fed rats during the first 25 days of 3'MeDAB feeding. High assays of urinary bile acids in 3'MeDAB-fed rats seemed to correlate with high rates of proliferation of oval cells in the livers of the rats.

2214 COMPENSATORY HYPERTROPHY ASSOCIATED WITH THE PRESENCE OF A DAB TUMOR IN THE RAT. (Fr.) Boy, M. J. (Natl. Ctr. Sci. Res., Paris, France), A. Jacob, H. H. Phan, P. C. Quan and E. Le Breton. *C R Acad Sci* 272(16):2093-2096, 1971.

Sprague-Dawley rats with dimethylaminoazobenzene (DAB)-induced hepatomas arising as a result of a DAB-supplemented diet administered over 3 months showed

significantly greater hepatic compensatory hypertrophy than did control rats with no tumors. Weights of excised livers (weight of hepatomas excluded) in rats fed DAB were greater than weights of livers of untreated control rats. The mechanism of this hypertrophy may involve augmented NADPH and ATP formation associated with increased synthesis of protein and lipid in the tumor-bearing animals.

- 2215 THE EFFECT OF INGESTA UPON DIMETHYLHYDRAZINE INDUCED-CARCINOGENESIS IN RAT COLON. (Ger.) Wittig, G. (Inst. Cancer Res., German Acad. Sci., Berlin), G. P. Wildner and D. Ziebarth. *Arch Geschwulstforsch* 37(2):105-115, 1971.

N,N-Dimethylhydrazine dihydrochloride (DMH) (10 mg/kg/wk s.c.) was administered to intact control rats and to a second group with the colon isolated from ingesta by a double-orifice descending colostomy. A third group with colostomy but without DMH-treatment served as control. All received a standard diet *ad lib*. Colonic carcinomas, distal benign and malignant tumors developed in 6 to 7 months. The co-carcinogenic action of ingesta was indicated by the significant difference in localization and frequency of colon carcinoma between the colostomy and unoperated animals.

- 2216 INCREASED TRANSFER RIBONUCLEIC ACID METHYLASE ACTIVITY IN TUMOURS INDUCED IN THE MOUSE COLON BY THE ADMINISTRATION OF 1,2-DIMETHYLHYDRAZINE. (E.) Pegg, A. E. (Middlesex Hosp. Med. Sch., London, England) and A. Hawks. *Biochem J* 122(1):121-123, 1971.

Transfer RNA methylase activity was assayed in colonic and rectal tumors induced in NMRI mice by 10 and 15 mg s.c. injections of 1,2-dimethylhydrazine. Mice were given weekly injections, and the first tumors appeared after 24 wk of treatment. Tumors were anal, colonic or rectal squamous cell carcinomas. Methylation of tRNA was measured in the presence of 0.05 mg of tRNA from *E. coli* K12. After incubation, the incorporation of methyl groups into material insoluble in 5% (w/v) trichloroacetic acid was determined. Normal mouse colon incorporated 75-79 pmole of methyl groups/15 min/mg protein, while colonic tumors incorporated 214-228 pmole of methyl groups/15 min/mg protein.

- 2217 EFFECT OF STRESS ON THE ADRENOCORTICOLYTIC AND CARCINOGENIC ACTION OF 7,12-DIMETHYLBENZ(a)ANTHRACENE. (E.) Somogyi, A. (Inst. Med. Exp. Surg., U. Montreal, Quebec, Canada) and K. Kovacs. *Z Krebsforsch* 75(4):288-295, 1971.

Female rats were exposed to stress before and after administration of either 7,12-dimethylbenz(a)-anthracene (DMBA), or 7-hydroxymethyl-12-methylbenz(a)-anthracene (7-OHM-MBA). "Stress" consisted of forced muscular exercise lasting for 6.5 hr, or forced muscular restraint lasting for 17 hr.

Although stress did not increase the incidence of adrenal lesions in rats given 4 mg DMBA, it was found that lesions which did appear in rats undergoing exercise stress prior to DMBA treatment were more severe than those appearing in rats not subjected to stress. The adrenal necrotic effect produced by 7-OHM-MBA was also potentiated by stress. Adrenal lesion incidence increased in rats given 4 mg of DMBA and prior exercise stress compared to rats given DMBA and no stress. In rats given 2 mg DMBA and restraint stress, spirolactone treatment nearly abolished the aggravation by stress of DMBA adrenalcorticolysis, while spirolactone had no such effect in rats given 4 mg of DMBA and restraint. In turn, stress was able to counteract the adrenal protection from the effects of DMBA afforded by spirolactone. The mammary carcinogenic effect of DMBA was not affected by stress.

- 2218 7,12-DIMETHYLBENZ(a)ANTHRACENE AND HEPATOPLASIA IN REGENERATING RAT LIVER. (E.) Marquardt, H. (Sloan-Kettering Inst. for Cancer Res., New York, New York), S. S. Sternberg and F. S. Phillips. *Chem-Biol Interact* 2(4):401-403, 1971.

Male rats were given i.v. injections of 7,12-dimethylbenz(a)anthracene (DMBA, 25 mg/kg) following partial hepatectomy, and the ensuing tumor incidence was compared with that in rats given DMBA without hepatectomy, and with that in hepatectomized rats not given DMBA. Among hepatectomized rats not given DMBA, the numbers of animals surviving for 300 days after the beginning of the experiment were 19 out of 20 in the group given no treatment and 19 out of 20 in the group given an injection of a control emulsion. Among hepatectomized rats given DMBA and intact rats given DMBA the numbers surviving after 300 days were 9/20 and 7/20, resp. No hyperplastic hepatic nodules developed among rats not given DMBA, while among hepatectomized rats given DMBA, 8 of 20 animals developed hyperplastic nodules. None of the intact and DMBA-treated rats developed hyperplastic nodules. One hepatectomized and DMBA-treated rat out of 20 developed a hepatocellular carcinoma; no carcinomas developed in any of the other groups. Among nonhepatic changes observed in DMBA-treated rats (intact and hepatectomized) were squamous papillomas, leukemia, osteogenic carcinomas and nerve tumors.

- 2219 EFFECTS OF LOCAL X-RAY IRRADIATION ON 7,12-DIMETHYLBENZ(a)ANTHRACENE-INDUCED CARCINOGENESIS. (Rus.) Karnaukhova, E. N. (Inst. Exper. Clin. Oncol. Acad. Med. Sci., U.S.S.R., Moscow) and V. S. Turusov. *Med Radiol* 16(2):75-77, 1971.

Cutaneous administration of 2 drops/wk for 4 weeks of a solution of 7,12-dimethylbenz(a)anthracene (DMBA) (total dose of 100 µg) to the dorsal skin of male hybrid mice (C57Bl X CBA/F₁) followed by local x-ray

sure to 1000 r produced an intensification of the chemical carcinogenic process only during the initial 4 month period. At later experimental intervals, a synergistic effect was observed with 100 µg of DMBA only when the radiation exposure was decreased to 500 r, and after 8 months the combined effects slightly delayed the carcinogenesis compared to the controls. The average number of papillomas per animal was highest (3.3) when the DMBA was combined with a dose of 500 r, somewhat lower with only DMBA (3.0), and significantly lower when the carcinogen was combined with a radiation exposure to 1000 and 2000 r (1.8 and 1.6, resp.). When the same carcinogenic dose was administered alone for 6 weeks, 93% of the animals developed tumors compared to only 64-70% in the animals receiving both the carcinogen and subsequent irradiation. The average number of papillomas per animal, the total number of tumors, and the absolute number of animals with tumors was actually highest in the control group and decreased as the radiation dosage increased in the group receiving the combined effects.

2220 MORPHOLOGICAL AND BIOLOGICAL FEATURES OF EXPERIMENTAL TUMORS OF THE CEREBELLUM IN RATS. (Rus.) Yablonskaya, L. Ya. (Inst. Human Morphol. Acad. Med. Sci. U.S.S.R., Moscow) and N. A. Spryskova. *Arkhh Pat* 33(2):50-53, 1971.

A model of primary intracerebellar neurocytoma was obtained by implantation of a 2 mg tablet of 7,12-dimethylbenz(a)anthracene into the right hemisphere of the cerebellum of Wistar rats. After an average latency period of 238 days, 17 of 22 rats developed tumors of the following morphological types: 3 astrocytomas, 5 dedifferentiated astrocytomas, 1 polymorphous glioblastoma, 3 oligodendroglioblastomas, 3 glioblastomas of mixed structure and 2 arachnoid endotheliomas. Three transplantable lines were established from passages by the intracerebellar method; they included 1 protoplasmic astrocytoma (with low malignancy), 1 fibrillar protoplasmic astrocytoma, and 1 strain of polymorphous glioblastoma of the highest malignancy.

2221 AN EPOXIDE IS AN INTERMEDIATE IN THE MICRO-SOMAL METABOLISM OF THE CHEMICAL CARCINOGEN, DIBENZ(a,h)ANTHRACENE. (E.) Selkirk, J. K. (McArdle Lab. Cancer Res., U. Wisconsin, Madison), E. Huberman and C. Heidelberger. *Biochem Biophys Res Commun* 43(5):1010-1016, 1971.

Evidence that an epoxide is produced in the microsomal metabolism of dibenz(a,h)anthracene (DBA) was obtained by heating microsomes to inhibit epoxide hydrolase. Microsomes from livers of Charles River rats that had been pretreated with 1 mg of methylcholanthrene 3 days prior to sacrifice (to induce the hydroxylating enzymes) were heated for 5 min at 50°C and then incubated at room temperature for 30 sec with ³H-DBA, MgCl₂, NADPH and unlabeled DBA-5,6-epoxide. Incubation was terminated by the addition of ethyl acetate. Thin layer chromatography of the

organic layer of the incubation mixture revealed the presence of an epoxide, characterized by its kinetics of appearance and disappearance, by its behavior on TLC and by its conversion under acidic conditions to the corresponding phenol. The probable role of epoxides as the activated metabolic and the ultimate carcinogenic derivatives of methyl group-lacking carcinogenic hydrocarbons is discussed.

2222 GLUCOSE-6-PHOSPHATE DEHYDROGENASE AND LACTATE DEHYDROGENASE ISOENZYMES IN RODENT MAMMARY CARCINOMAS AND THE EFFECT OF OOPHORECTOMY. (E.) Richards, A. H. (U. Rochester School of Med. and Dentistry, New York) and R. Hilf. *Biochim Biophys Acta* 232(4):753-756, 1971.

Oophorectomy was performed on 7,12-dimethylbenz(a)-anthracene (DMBA)-induced mammary tumor-bearing Sprague-Dawley rats to ascertain whether the procedure would produce preferential effects on specific isoenzyme species. Rats were administered 5 mg DMBA/ml in sesame oil once a wk for 5 wk; tumors developed 8-12 wk after initial feeding of the carcinogen. The animals were then divided into groups according to approximate tumor size, and oophorectomy was performed under ether anesthesia; neoplasms were removed 3 or 5 days following oophorectomy for enzyme determinations. The average weights of the investigated tumors were: 1.5 g in intact rats, 2.2 g 3 days after oophorectomy and 2.4 g 5 days after oophorectomy. Glucose-6-phosphate dehydrogenase in the neoplasms was found to have 2 major isoenzymes, a fast-moving band designated as F, which constituted 85% of the total activity, and a slower-moving band designated as S. The activity levels of glucose-6-phosphate dehydrogenase were 8.6, 7.8 and 4 units per 100 mg at 0, 3 and 5 days after oophorectomy, resp. This decrease appeared to be due entirely to a decrease in the activity of glucose-6-phosphate dehydrogenase F, the hormonally responsive isoenzyme in these tumors. Lactate dehydrogenase activity decreased from 158 units (intact rats) to 131 units and 111 units per 100 mg 3 and 5 days following surgery. The isoenzymes lactate dehydrogenase-5 and -4 decreased from 1.4 units to 1.1 and 0.6 units and from 0.7 units to 0.4 and 0.4 units per mg DNA, resp., 3 and 5 days following surgery. These isoenzymes were of the muscle type, M₄ and M₃H₁ resp. The mammary carcinomas appeared to contain very low levels of the heart-type lactate dehydrogenase isoenzymes.

2223 HORMONE-INDUCED FUNCTIONAL RESPONSE IN MAMMARY GLANDS AND MAMMARY TUMOURS. (E.) Heise, E. (German Acad. Sci., Berlin-Buch, Germany), M. Görlich, Ch. Kleitke and G. Bacigalupo. *Europ J Cancer* 7(1):71-76, 1971.

Lactose was assayed in normal rat mammary glands, in mammary glands of rats given p.o. doses of 20 mg dimethylbenzanthracene (DMBA), and in hormone-stimulated mammary glands. Mammary glands of pregnant rats, transplanted fibroadenomata, and human mammary glands did not contain lactose. Lactose

was present in 2 of 24 DMBA-induced mammary carcinomas and in 5 of 33 DMBA-induced fibroadenomas. In rat mammary glands bearing DMBA-induced fibroadenomas, the content of lactose could be increased by treating the rats with hormones; 38.5% of rats bearing DMBA-induced fibroadenomas which were given testosterone treatment were lactose-positive in mammary tissue, 40.0% of tumor-bearing rats given estradiol had lactose, and 66.6% of tumor-bearing rats given estradiol-and-progesterone treatment had lactose-positive mammary tissue. Testosterone treatment induced lactose in normal mammary glands of pregnant rats, as did ovariectomy performed before parturition.

- 2224 BINDING OF [G-³H]-7,12-DIMETHYLBENZ(a)-ANTHRACENE TO DNA OF NORMAL AND OF RAPIDLY DIVIDING HEPATIC CELLS OF RATS. (E.) Marquardt, H. (McArdle Lab. Cancer Res., U. Wisconsin, Madison), A. Bendich, F. S. Philips and D. Hoffmann. *Chem Biol Interact* 3(1):1-11, 1971.

CD-line rats were injected i.v. at 24 hr after partial hepatectomy with ³H-7,12-dimethylbenz(a)anthracene (DMBA) in doses of 5 mC/120 µg/kg; they were killed 6 hr later, and the DNA isolated from regenerating liver had a specific activity after purification of 2 µC/g of DNA which represented binding of 2×10^{-10} moles of DMBA/g DNA or about 100 molecules of DMBA to the genome of one regenerating liver cell. The binding after 25 mg/kg i.v. was equivalent to 20,000 molecules of DMBA per liver cell genome. The binding of DMBA to DNA of regenerating rat liver and small intestine 1 hr after i.v. injection was negligible, but after 3 hr the binding to intestinal DNA was nearly maximal and that to regenerating liver DNA was about 50% of the maximum reached at 6 hr; this maximum was 4 times greater than that seen in intact liver of young adults. In the small intestine, the binding did not change appreciably between 6 and 48 hr, but in the regenerating liver the amount of DMBA bound to DNA dropped considerably between 6 and 24 hr. DNA isolated from regenerating liver 24 hr after partial hepatectomy bound about 2.5 times as much DMBA *in vitro* as that isolated from liver of young adults; prior activation of the DMBA did not seem to be required for tight binding under the conditions of this experiment. Gas chromatographic analysis of the DMBA-DNA complexes did not provide any evidence for the presence of covalent derivatives of DMBA.

- 2225 EFFECT OF POLYINOSINIC-POLYCYTIDYLIC ACID ON INDUCTION OF PRIMARY OR TRANSPLANTED TUMORS BY CHEMICAL CARCINOGEN OR IRRADIATION. (E.) Ball, J. K. (Cancer Res. Lab., U. Western Ontario, London, Ontario, Canada) and J. A. McCarter. *J Natl Cancer Inst* 46(5):1009-1014, 1971.

Mice of the CFW/D strain were given injections of polyinosinic-polycytidylic acid (poly I:C) 12-16 hr before a single neonatal injection of 25 µg of 7,12-dimethylbenz(a)anthracene (DMBA). Mice pretreated with poly I:C showed an increased mortality from thymic lymphomas compared to mice given DMBA

alone; by 150 days after treatment, all mice given DMBA and poly I:C had died with lymphomas, while 50% of mice given DMBA only survived. Poly I:C pretreatment reduced the incidence of thymic lymphomas induced by a neonatal exposure to 400 rads whole-body X-irradiation. Tumor incidence in mice exposed to X-irradiation and not treated with poly I:C was 94% while tumor incidence in mice pretreated with poly I:C and exposed to X-rays was 40%. Poly I:C treatment showed an antitumor effect on transplantation of thymic lymphomas when both tumor cells and poly I:C were administered i.p.; when poly I:C and tumor transplant cells were administered according to different protocols no antitumor protective influence was seen. In some cases, poly I:C appeared to enhance tumor development in mice given trans-

- 2226 REGRESSION OF PROLACTIN-DEPENDENT RAT MAMMARY CARCINOMA IN RESPONSE TO ANTIHORMONE TREATMENT. (E.) Butler, T. P. (Dept. Med., Case Western Reserve U. Sch. Med., Cleveland, Ohio) and O. H. Pearson. *Cancer Res* 31(6):817-820, 1971.

Mammary tumors were induced in female rats by intragastric administration of 7,12-dimethylbenz(a)anthracene (DMBA), and anti-prolactin antiserum was produced in rabbits using rat prolactin. Tumor-bearing rats were given s.c. or i.p. injections of anti-prolactin antiserum twice daily for 36 days (1 ml of 1/12,000 titer antiserum daily for 13 days, 0.5 ml of 1/32,000 titer antiserum daily for 19 days and 0.4 ml of 1/64,000 titer antiserum daily for 4 days). Fifty percent of the tumors in anti-prolactin-treated rats and 13% of the tumors in rats given normal rabbit serum regressed. Thirty-five percent of the tumors in anti-prolactin-treated rats and 57% of the tumors in untreated rats grew. Tumors in treated rats resumed growth after anti-hormone treatment had been discontinued. After 36 days of treatment tumor areas in untreated rats amounted to more than 6 cm² compared to tumor areas in anti-hormone treated rats of about 3 cm².

- 2227 MAST CELLS IN THE 7,12-DIMETHYLBENZ(a)-ANTHRACENE INDUCED MAMMARY TUMORS IN RATS. (Ger.) Kovacs, K. (Inst. Exp. Med. Surg., U. Mo. Canada) and A. Somogyi. *Zbl allg Path* 114(1):69-71, 1971.

The effect of 7,12-dimethylbenz(a)anthracene (DMBA) on the accumulation of mast cells was investigated before and after tumor induction. In the untreated animals, the few mast cells present were distributed in the tubules and alveoli of the mammary glands in the fat and connective tissue at times. Four days after the administration of a single dose of DMBA by gavage, mast cells were found to be slightly increased in number and were distributed similarly to the untreated animals. Not all the animals receiving the DMBA tumors. The number of mast cells in those tumors that developed 2-3 months after DMBA varied and was very abundant in some, while in others there were only slightly more mast cells than were found in

treated animals; they occurred mainly in the connective tissue and were unevenly distributed. Triclinolone, compound 48/80 and polymyxin, each administered repeatedly for 2-3 months after DMBA-induced tumors occurred, caused a reduction in the number of mast cells. The role of these cells in carcinogenesis is not known.

8 CARCINOGENICITY OF AIRPLANE ENGINE SOOT IN EXPERIMENTAL ANIMALS. (Rus.) Linnik, A. (Inst. Exp. Clinical Oncol. Acad. Med. Sci., Moscow, U.S.S.R.), G. A. Smirnov and L. M. Shabad. *Bull Eksp Biol Med* 71(2):83-87, 1971.

Extracts of soot from airplane turbines and pistons containing benzo(a)pyrene concentrations of 25 mg/kg and 30 mg/kg, resp., applied twice a wk for 1 month and then 3 times/wk for a total of 50 applications to the interscapular region of the skin of 1st generation hybrid mice (C57 X CBA), produced tumors in 58 of the 66 treated animals; 28 of 34 control animals treated similarly with a 0.1% solution of benzo(a)pyrene also developed neoplasms; a fourth group of 20 mice received pure benzene and did not develop any neoplasms. Histologically, confirmed squamous cell carcinoma of the skin developed in 52 of the 58 animals, sarcoma in 1 mouse and carcinoma in 4 mice; lymph node cancer metastasis was observed in 6 cases. The results suggest that benzo(a)pyrene concentration may serve as an indicator of the carcinogenic potency of soot and similar products.

9 IN VITRO CELLULAR UPTAKE OF BENZO(a)PYRENE MEASURED BY A MICROFLUOROMETRIC TECHNIQUE. Kouri, R. E. (Roche Inst. Molec. Biol., Nutley, N.J.), R. A. Lubet and D. Q. Brown. *Proc Soc Exp Biol Med* 136(4):1038-1044, 1971.

Cell line derived from lung tissue of the Chinese hamster was incubated with 0.05% of benzo(a)pyrene and BP uptake was measured by a microfluorometric technique. Cells that were pretreated with 0.6 µg/ml BP for 12 hr and incubated for 1 hr without BP prior to toxicity experiments showed an increase in uptake of BP at 0.5, 3.0, 5.0, 11.0 and 24.0 hr periods compared to non-pretreated cells. The ability to uptake the chemical was correlated with its induced toxicity. A lysosomal extrusion process appeared to be operative at low concentrations of BP.

EFFECT OF OZONE ON BENZOPYRENE HYDROXYLASE ACTIVITY IN THE SYRIAN GOLDEN HAMSTER. Palmer, M. S. (Environmental Protection Agency, Air Pollution Control Off., Div. Hlth. Effects Res., Cincinnati, O.), D. H. Swanson and J. Coffin. *Cancer Res* 31(6):730-733, 1971.

Animals of both sexes were exposed to ozone for 3 weeks after which benzo(a)pyrene (BP) hydroxylase activity in the lungs of exposed animals was determined. In hamsters not exposed to ozone, the

BP hydroxylase activity in the lung was 0.09 U of enzyme activity/mg wet weight of tissue; in animals exposed to 1,470 µg/m³ of ozone, enzyme activity was 0.06 U/mg, and in animals exposed to 5,880 and 19,600 µg/m³ of ozone, enzyme activity was 0.03 U/mg. Exposure to ozone did not affect BP hydroxylase activity in the liver of hamsters. When hamsters were pretreated with 10 mg BP prior to ozone exposure, lung BP hydroxylase activity was increased by as much as 70-fold; however, values for enzyme activity were still significantly lower in ozone-treated hamsters than in controls. Lungs of hamsters given BP and not exposed to ozone showed 6.6 U enzyme activity/mg tissue assayed, while hamsters given pretreatment and 1,470 µg/m³ ozone showed 4.3 U/mg. Hamsters given BP pretreatment and 5,880 µg/m³ ozone showed 1.8 U/mg BP hydroxylase activity. It was thought that ozone acted to delay the enzymatic transformation of inhaled BP, thus functioning as a cocarcinogen for this agent.

2231 TRANSPLACENTAL ACTION OF BENZ(A)PYRENE AND PYRENE IN MOUSE EMBRYO KIDNEY TISSUE CULTURES. (Rus.) Sorokina, Yu. D. (Inst. Exp. Clin. Oncol. Acad. Med. Sci. U.S.S.R., Moscow). *Bull Eksp Biol Med* 71(3):72-76, 1971.

The transplacental action of benzo(a)pyrene (BP) in (C57BLxCBA)F₁ mouse embryo kidney tissue cultures was investigated. BP or pyrene (P) were administered (1 mg in olive oil 4 times, i.m.) during the last wk of pregnancy and embryo explants were taken on the 20-21st day of pregnancy. The survival time of tissue cultures from both experimental groups appeared to be higher than that of the untreated explants. Ninety-eight percent of the untreated embryo, 54% of the P-treated and 47% of the BP-treated embryo tissue cultures were depleted 22 days after the explant. The hyperplastic alterations consisted of minor epithelial atypia and constituted 1.8% of the total number of control explants. A considerably higher degree of atypia within the hyperplastic alterations (18.0% in the P-treated and 27% in the BP-treated embryo tissues) along with hyperplasia of isolated canaliculi and structureless epithelial blast cells were observed in the treated embryo tissues. Diffuse epithelial hyperplasia, partial or total disappearance of canalicular structure and the formation of blast cells were observed in 9 (75%) of the BP-treated explants on the 22nd-30th day after explant. Such effects were not seen in the P-treated explants.

2232 THE USE OF FREUND'S ADJUVANT IN THE PRE-CANCEROUS STAGE: ITS EFFECT ON CHEMICAL CARCINOGENESIS. (Rus.) Volegov, A. I. (P. A. Herzen Sci. Res. Inst. Oncol., U.S.S.R., Moscow). *Bull Eksp Biol Med* 71(2):79-81, 1971.

Freund's complete adjuvant (FA) administered into the pad of the left paw in 16 Wistar rats (0.03 ml) 80 days following the s.c. administration of 3 mg of 3-methylcholanthrene (MC) reduced the resistance of the animals to the carcinogenic effect of the com-

pound. Histologically confirmed polymorphocellular sarcoma developed in the FA + MC-treated rats; in control rats without FA treatment, MC induced only spindle or polymorphic cells. A third group of rats administered 0.03 ml of Freund's adjuvant s.c. into the abdominal region had neoplasms of an intermediate grade of malignancy. The first neoplasms appeared 3½ months after administration of the carcinogen; animals receiving the adjuvant in the paw had a significantly higher incidence of tumors at 5½ months; however, at all other experimental times, there were no significant differences among the 3 groups. FA induced polyarthritis only in 8 of the 16 rats receiving the paw injection; however, no correlation could be observed between the appearance of the polyarthritis and the decreased resistance to the oncologic process. The effect of FA seemed to be associated with the development of an autoimmune process in the organism of the animals.

- 2233 THE EFFECT OF ERYTHROPOIETIN ON THE DEVELOPMENT OF 20-METHYLCHOLANTHRENE-INDUCED SKIN TUMORS. (Rus.) Finogenova, M. A. (Inst. Nutr. Acad. Med. Sci. U.S.S.R., Moscow). *Pat Fiziol Exp Ter* 15(1):41-45, 1971.

The effect of erythropoietin-containing serum (EPS) on the development of skin tumors induced by 3-methylcholanthrene (MC) was studied in CBAXC57BL male and female mice. MC was applied topically (0.02 ml as a 0.05% benzene soln) in the intercostal region and EPS, obtained from rando-bred rats, was administered simultaneously (0.5 ml/EPS, i.p.) once a wk for 5 wks; another group received additionally for 5 more wk a double dose of EPS. A second series of experiments was carried out in mice treated with a 1% croton oil in benzene soln (0.02 ml once a wk for 20 wk), starting 2 wk after a single dose (0.04 ml) of MC application; various groups received 1 ml EPS the day before, the day of and the day after MC or croton oil application. In a third series MC (0.02 ml single dose) application was followed 30 days later by 1% croton oil treatment (0.02 ml once a wk) through the 20th wk of the experiment; EPS was given (1 ml i.p. once in 5 days) for 30 days after the MC application. EPS decreased the latency period for MC induction of the 1st papilloma by 3 wk, (from wk 11 to wk 8) and the development of malignancy by 2 wk (from wk 20 to wk 18) compared to the mice receiving normal serum within the first series of experiments; additional EPS treatment decreased the latency for the occurrence of the first papilloma and the development of the first malignancy by 1 wk only. EPS treatment increased the number of animals with papillomas by 23% on the 14th wk and by 29% on the 20th wk and had no effect on the latency period in the second experimental series (1% croton oil, MC and 3 doses of EPS). The incidence of papillomas was increased by 23-30% in the third experimental series (1% croton oil, MC and 6 doses of EPS), while the occurrence of the 1st papilloma and the malignization were hastened by 2 wk. The enhancing effects of EPS appeared to be more manifest during the early stages of carcinogenesis with or without cocarcinogen; its effects

appeared to be minor during the activation stage and stronger in females.

- 2234 THE EFFECT OF VITAMIN B₁₂ ON THE INDUCTION OF SKIN TUMORS IN MICE. (Rus.) Ostryanina, A. D. (Inst. Nutr. Acad. Med. Sci. U.S.S.R., Moscow). *Pat Fiziol Exp Ter* 15(1):48-51, 1971.

The effect of vitamin B₁₂ on 3-methylcholanthrene (MC) skin carcinogenesis was studied in 807 CBAXC57BL male mice. MC was applied topically to the intercostal region as a 0.05% benzene soln once a wk for 12-24 wks. Vitamin B₁₂ was administered s.c. (20, 40 or 200 µg/kg) 3 times a wk as follows: I) 4 wk before MC treatment, II) 4 wk before and during MC treatment up to the development of the papilloma (10 wk), III) during the MC treatment for 10 wk, IV) as in III with 2 wk intervals after each month, or V) after the occurrence of the 1st papilloma (following 12 wk of MC treatment) for 1 or 12 wk. An enhancement of carcinogenesis was seen when vitamin B₁₂ treatment was started simultaneously with MC application (III). The 20 or 40 µg/kg dose of vitamin B₁₂ reduced the latency period by 1 wk and the 200 µg/kg dose reduced the latency by 2 wks. Similar results were noticed in the enhancement of malignant transformation of the papillomas. When given after the occurrence of the 1st tumor (V) or during the MC treatment with 2 wk intervals (IV), vitamin B₁₂ doses of 20 and 40 µg/kg produced a marked enhancement of malignant transformation. No effects were seen, however, when the vitamin was administered prior to and/or continuously during the period of MC application (I, II); this may be due to a state of vitamin B₁₂ saturation.

- 2235 THE INFLUENCE OF MUCOUS SECRETION ON THE INDUCTION OF UTERINE CERVICAL CARCINOMA IN MICE OF THE STRAINS BN, PORTON AND A. (E.) Gorski, T. (Inst. Oncol., Gliwice, Poland) and W. Smieciński. *Folia Biol* 17(1):75-82, 1969.

Pellets of beeswax impregnated with methylcholanthrene (MC) were placed intravaginally in mice of strains A, Porton and BN. In some mice, a ligature was placed in the vagina below the MC pellet resulting in an increase in mucous moistening; in other mice the ligature was placed in the vagina above the pellet resulting in a decrease in mucous moistening. In BN and Porton mice treated with MC the incidence of cervical carcinoma was lower in controls with vaginal ligature than in mice with ligatures; carcinoma incidence was higher in mice with ligatures above the MC and also higher in mice with ligatures below the pellet. However, in mice of strain A with the ligature placed above the pellet, carcinoma incidence was lower than in MC-treated mice without ligatures.

- 2236 CHROMOSOMES OF CHEMICALLY INDUCED TUMORS AFTER TUMOUR POLYPASSAGE. (E.) Popescu, N. C. (Acad. Med. Sci., Bucharest, Romania) and I. Cioloca. *Neoplasma* 18(1):15-18, 1971.

tumors induced in hamsters by 3-methylcholanthrene were implanted s.c. into recipient hamsters 6 times at 48 hr intervals; after 6 transplantations the tumor fragments were allowed to grow for 14 days and then analyzed chromosomally. Cells from tumors which had been repeatedly transplanted to a host designated "polypassaged" tumor cells) were predominantly diploid; on the other hand, tumors which had not been polypassaged were predominantly tetraploid. Tumors were originally induced in male hamsters, and polypassaged in female hamsters, and the percentage of host cells with female karyotypes in polypassaged tumors was 33-40%.

237 CHEMICAL AND ENZYMIC COMPOSITION OF MICROSOMAL SUBFRACTIONS FROM RAT LIVER AFTER TREATMENT WITH PHENOBARBITAL AND 3-METHYLCHOLANTHRENE. (E.) Glaumann, H. (Karolinska Inst., Stockholm, Sweden). *Chem-Biol Interact* 2(4):369-380, 1970.

Phenobarbital (8 mg/100 g body wt) once daily for 5 days and 3-methylcholanthrene (2 mg/100 g) on day 4 and 2 prior to the experiment were administered i.p. to starved adult male albino rats and the distribution of protein, RNA, phospholipids and cholesterol was determined among microsomal subfractions of rough, smooth I and smooth II membranes. Phenobarbital increased the protein, phospholipid and cholesterol content in total, rough, and in smooth I subfractions in particular. No increase in either protein or lipids of the smooth II microsomes was seen, and although there were quantitative differences, the response in the rough subfraction paralleled that in smooth I membranes. In contrast, 3-methylcholanthrene did not enhance the content of either protein or lipids in any of the microsomal subfractions. Phenobarbital caused some decrease in the activities of glucose-6-phosphatase, ATPase, and AMPase recovered from total, rough and smooth I microsomes and increased nucleoside diphosphatases in these same fractions; 3-methylcholanthrene failed to change these activities except for a moderate increase in nucleoside diphosphatase activity in the rough and smooth I microsomes.

238 THE INFLUENCE OF BCG VACCINE AND GROWTH OF METHYLCHOLANTHRENE-INDUCED TUMOR ON THE STRUCTURE OF THE RETICULO-HISTIOCYTE SYSTEM OF LIVER AND SPLEEN IN RATS AND MICE. (Ger.) Wolf, G. (Inst. Cancer Res., German Acad. Sci., Berlin), N. Schremmer and K. H. Horn. *Arch Geschwulstforsch* 37(2):152-160, 1971.

Transplantation of methylcholanthrene-induced tumor tissue into 3-month-old male and female rats was followed by significant hyperplastic changes in the liver and spleen within 5-13 days. S. C. injection of BCG vaccine either concomitantly with or 14 days preceding tumor transplants did not affect these changes; nor did BCG vaccine alone have any demonstrable morphologic effect on these 2 organs. Tissue changes were examined under light and electron microscopy; splenic lympho-reticular structure hyperplasia and enlargement of Kupffer cells were observed.

2239 CARCINOGENIC ACTION OF NITROSAMINES IN MICE. (Rus.) Shabad, L. M. (Inst. Exp. Clin. Oncol. Acad. Med. Sci. U.S.S.R., Moscow) and L. A. Savluchinskaya. *Biull Eksp Biol Med* 71(3):76-78, 1971.

The effect of dimethylnitrosamine (DMNA), diethylnitrosamine (DENA) and nitrosomethylurea (NMU) in 104 (54 male and 50 female) A and 117 (67 male and 50 female) C3HA mice, 2-months-old, was investigated. The carcinogens (0.1 mg) were administered s.c. twice a wk for 3 wk each or p.o. 3 times a wk for 8-12 wk. The first tumor (adenocarcinoma of the lung) was noticed in a C3HA mouse 12 months after s.c. treatment and 7 months after p.o. treatment (adenoma of the lung). Lung and liver appeared to be the main target organs. The adenomas of the lung were usually multiple and of the mixed type with a well differentiated core and the cells contained hyperchromic oval nuclei. The liver tumors appeared to be benign (simple or multiple) with large cells and hyperchromic nuclei; 9 mice had hepatocellular malignancies with infiltrative growth and polymorphic cells. DENA induced the highest number of malignancies of the cardia (10 of 34 C3HA mice); DMNA induced cystadenomas of the kidney in 7 of 54 C3HA mice and 1 giant adenoma (kidney in 1 animal). The cystadenomas appeared to be a third stage of transformation after hyperplasia and focal proliferation that developed into adenocarcinoma or cystadenocarcinoma. The highest incidence of tumors was induced by NMU (58-92%); the incidence of tumors in the overall experiment was 34-93%. There was no difference in susceptibility of the 2 strains A and C3HA towards DMNA or NMU; the C3HA strain seemed to be somewhat more susceptible to DENA, and 29% of them developed malignancies of the cardia. No substantial differences between the action of the 3 carcinogens were observed, however.

2240 TOXICITY OF DIMETHYLNITROSAMINE FOR THE RAT TESTIS. (E.) Hard, G. C. (Med. Res. Counc. Lab., Carshalton, Surrey, England) and W. H. Butler. *J Path* 102(4):201-207, 1970.

Male rats were maintained on a protein-supplemented or a protein-free diet and were given a single i.p. injection of either 30 or 60 mg/kg of dimethylnitrosamine (DMN); the effects of DMN on testicular tissue were observed in the 2 dietary groups. Rats given 60 mg/kg DMN and maintained on a protein-free diet showed degenerate changes in the spermatids of many testicular tubules. Twenty-four hours after injection occasional multinucleate giant cells containing nuclei of spermatid origin were seen. Degenerative changes progressed during the next few days, involving spermatocytes and spermatogonia; by the second day, all tubules were uniformly affected. Spermatids at this stage showed karyorrhexis, karyolysis or pyknosis of nuclei. At 4 days spermatozoa were absent and spermatocytes were rare. The peak of degenerative change was seen at 7 days; after 2 wk, most rats showed progressive regeneration of seminiferous epithelium, and multinucleate cells had disappeared. By 4 wk, spermatogenesis was largely restored. In rats given 60 mg/kg DMN and

maintained on a protein-supplemented diet, changes were less pronounced than in the protein-free dietary group. Thirty mg/kg DMN produced less marked changes in rats given a protein-free diet than did 60 mg/kg. The testes of rats given 30 mg DMN and a protein-supplemented diet showed no significant changes.

- 2241 NITROSAMINE STUDIES: INDUCTION OF LUNG ADENOMAS BY CONCURRENT ADMINISTRATION OF SODIUM NITRITE AND SECONDARY AMINES IN SWISS MICE. (E.) Greenblatt, M. (U. Nebraska Coll. Med., Omaha), S. Mirvish and B. T. So. *J Nat Cancer Inst* 46(5):1029-1034, 1971.

Swiss strain mice were maintained for 40 wk on a diet containing one of the following chemicals: piperazine (6.25 g/kg of food), morpholine (6.33 g/kg food), N-methylaniline (1.95 g/kg food), dinitrosopiperazine (40 mg/liter of drinking water), dimethylamine hydrochloride (5.9 g/kg food), nitrosomorpholine (80 mg/liter water), dimethylnitrosamine (10 mg/liter water) or N-nitroso-N-methylaniline (70 mg/liter water). Chemicals were administered with sodium nitrite (1 g/liter) in drinking water. Piperazine, morpholine and N-methylaniline increased the incidence of lung adenomas, especially in male mice. Dinitrosopiperazine, nitrosomorpholine, dimethylnitrosamine and N-nitroso-N-methylaniline produced a 10-30-fold increase in lung adenomas in treated as compared to untreated mice. Neither dimethylamine hydrochloride nor sodium nitrite alone nor secondary amines alone caused an increase in tumor incidence.

- 2242 DIETHYLNITROSAMINE-INDUCED ALTERATIONS IN THE TRACHEOBRONCHIAL SYSTEM OF SYRIAN GOLDEN HAMSTERS. (E.) Althoff, J. (U. Nebraska Med. Ctr., Omaha), R. Wilson and U. Mohr. *J Nat Cancer Inst* 46(5):1067-1071, 1971.

Ten male and 10 female golden hamsters were given s.c. injections of 10 mg/kg diethylnitrosamine and the ensuing changes in the tracheobronchial system were observed under an electron microscope. Papillary tumors developed in all hamsters given the carcinogen. Prior to the development of papillary tumors, hyperplasia and dysplasia were seen in epithelial tissue; tumor epithelium also showed hyperplasia and dysplasia. Squamous epithelium showed no metaplastic change, either in the tracheobronchial tissue or in tumor epithelium.

- 2243 CYTOGENETIC STUDIES IN SPRAGUE-DAWLEY RATS DURING THE ADMINISTRATION OF A CARCINOGENIC NITROSO COMPOUND--DIETHYLNITROSAMINE. (E.) Grover, S. (Med. Coll., Nagpur, India) and P. Fischer. *Europ J Cancer* 7(1):77-82, 1971.

Newborn rats were given daily s.c. injections of diethylnitrosamine (DEN), in a dose of 10 mg/kg of body wt, for up to 48 days. Cytogenetic studies

were performed on liver and spleen cells from treated animals. Until day 3 of carcinogen treatment, karyotypes from spleens and livers of treated rats did not differ from those of untreated rats. On day 3, however, 9 of 126 metaphases studied were pseudodiploid with a small metacentric or submetacentric chromosome and an increased number of small acrocentric chromosomes. By day 48 of DEN treatment, liver cell chromosomes were sticky and elongated with a tendency to non-disjunction and fusion. Of 4 karyotypes from this material showed a missing A7 chromosome and an extra small acrocentric. Nodules were found on livers of rats sacrificed after 60 days on the carcinogenic regimen, and karyotypes of cells from these nodules showed similar patterns to karyotypes of cells from rats treated with carcinogen for 48 days.

- 2244 DIFFERENCE IN THE ONCOGENICITY OF N-METHYL-N-NITROSO- β -D-GLUCOSYLAMINE, N-METHYL-N-NITROSO- β -D-GALACTOSYLAMINE AND ANALOGOUS SUGAR ALCOHOLS IN RATS. (Ger.) Güttner, J. (Central Inst. Microbiol and Exp. Ther., Jena, Germany), A. Schmidt and W. Jungst. *Z Krebsforsch* 75(4):296-300, 1971.

Four groups of 10-13 wk-old Wistar rats (4 males and 4 females each) were administered p.o. 50, 460, or 1800 mg/kg of N-methyl-N-nitroso- β -D-glucosylamine or alcohol analog and 24 animals (males or females) were given 750 mg/kg N-methyl-N-nitroso- β -D-galactosylamine or alcohol analog twice weekly for 25 wk. Both MN-glucosylamine and its alcohol analog induced hepatomas (in 10 and 9 rats, resp.) and phrenic ampulla papillomas (in 12 and 13 rats, resp.). No significant differences in their effects due to the different dosages were seen. The alcohol analog induced additional tumors of the larynx, pharynx and esophagus in 21 rats. The total MN-glucosylamine induced tumor incidence was 58% and that induced by its alcohol analog was 91%. MN-galactosylamine and its alcohol analog induced no histologically detectable tumors through the 322nd day of the experimental period.

- 2245 STIMULATION OF THE RATE OF INDUCTION OF LUNG TUMORS BY DIETHYLNITROSAMINE IN MICE. (Ger.) Hilfrich, J. (Path. Dept., U. Hamburg Med. Sch., Germany), J. Althoff and U. Mohr. *Krebsforsch* 75(3):240-242, 1970.

Administration of 50 mg/kg of diethylnitrosamine s.c. once or twice weekly for 4 wk (total dose of 200 or 400 mg/kg, resp.) to male and female mice elicited a 2-3-fold increase over controls in rate of lung adenoma formation with significant decreased latency periods within 6-12 months of treatment. Although there was a 60% mortality with marked hepatic damage after 2 months at the higher dose level, no significant difference in tumor formation was found between the 2 dosage groups. Hepatomas, papillomas of the forestomach and squamous cell carcinoma of the nasopharyngeal cavity were also observed in diethylnitrosamine-treated animals.

46 STUDIES ON LUNG TUMOURS: II. MORPHOLOGICAL ALTERATIONS INDUCED BY DIMETHYLNITROSAMINE IN MOUSE LUNG AND LIVER AND THEIR RELEVANCE TO CARCINOGENESIS. (E.) Calafat, J. (The Netherlands Cancer Inst., Amsterdam), L. den Engelse and P. Melot. *Chem-Biol Interact* 2(4):309-320, 1970.

Ultrastructural changes in the livers and lungs of C57BL/6 and C3Hf mice given a single i.p. injection of 10 mg/kg dimethylnitrosamine (DMNA) were observed 24 hr after administration of the carcinogen. DMNA produced similar changes in both mouse strains. Cytoplasmic changes were first seen in liver cells, and nuclear changes were seen first in lung cells. 24 hr after treatment, the endoplasmic reticulum in bronchiolar epithelial lung cells showed a concentric arrangement surrounding 1 or more mitochondria. In the nuclei of some liver cells, dark plaques were seen 1 hr after injection. By 2.4 hr, nucleolar components were arranged into a fibrillar zone, a smaller granular zone and a dark peripheral zone. The peripheral dark zone and plaques were similar to inclusions seen after treatment of mice with 4-nitroquinoline-N-oxide, lasiocarpine or aflatoxin. EDTA staining suggested that the dark-staining components of the nucleolus were composed of protein. Nucleolar components were also rearranged in the bronchiolar epithelium of lungs of DMNA-treated mice. These results did not reveal a clear relationship between the morphological and carcinogenic effects of DMNA in the lung or liver of the mouse.

47 HISTOCHEMICAL ACTIVITY OF ALKALINE AND ACID NUCLEASES IN THE RAT LIVER PARENCHYMA DURING N-NITROSOMORPHOLINE CARCINOGENESIS. (E.) Ober, H. S. (Dept. Gen. Path., U. Louvain, Belgium), Fort and J.-M. Brucher. *Cancer Res* 31(6):913-916, 1971.

Young male albino rats were given 8 mg/kg N-nitrosomorpholine by intragastric intubation 5 times daily, and the localization in the liver of alkaline and acid DNase and RNase was observed. In rats killed after 38 days on the carcinogenic regimen, levels of acid and alkaline nucleases were nearly normal in the liver. After 59 days of treatment, large areas of liver parenchyma cells with clear cytoplasmic vacuoles could be seen; acid nuclease activity was markedly decreased in some groups of liver cells, while alkaline nuclease activity was only slightly reduced. By 78-85 days of carcinogen treatment, macroscopic nodules had begun to appear in the livers of treated rats; these nodules had distinctly reduced acid and alkaline nucleases. By 100 days of carcinogen treatment, the nodules had enlarged and acid nuclease activity in them was practically nil. However, acid nuclease was present in the surrounding liver parenchyma cells. Alkaline nuclease was also nearly absent in the nodules and present in surrounding parenchyma cells. By 134 days of treatment, signs of malignant transformation were present in livers; areas of malignancy revealed acid or alkaline DNase or RNase. However, intense nuclease activity was seen in the peripheral zones of necrotic foci.

2248 QUANTITATIVE ASPECTS OF THE REPAIR OF ALKYLATED DNA IN CULTURED MAMMALIAN CELLS: I. THE EFFECT ON HeLa AND CHINESE HAMSTER CELL SURVIVAL OF ALKYLATION OF CELLULAR MACRO-MOLECULES. (E.) Roberts, J. J. (Roy. Cancer Hosp., London, England), J. M. Pascoe, J. E. Plant, J. E. Sturrock and A. R. Crathorn. *Chem Biol Interact* 3(1):29-47, 1971.

Single cell suspension cultures of HeLa S3, a human female tumor line, and Chinese hamster V79-379A cells were treated with varying concentrations of N-methyl-N'-nitro-N-nitrosoguanidine (MNNG), N-methyl-N-nitrosourea (MNU), methyl methanesulphonate (MMS), mustard gas or half mustard gas for 1 hr. Concentrations of MNNG, MNU, and MMS required to kill 90% of the HeLa cells were in the ratio of 1:200:2000, while for hamster cells the corresponding ratios were 1:100:150. Ion-exchange chromatography for acid-hydrolyzed DNA from both cell lines with labeled MNNG, MNU and MMS indicated that virtually all the radioactivity eluted from the column was associated with the absorbance corresponding to 7-methylguanine, and there was no evidence for metabolic incorporation of radioactivity into the purines. A clear linear relationship existed between the reaction of hamster cell DNA with the alkylating agents and the concentration of the three agents. Treatment of HeLa cells with the MNU and the MNNG showed that for a given toxicity the binding of alkylating agent to DNA was very much less than predicted with a non-linear relationship of the dose-binding curves; with HeLa cells and MMS results similar to those seen in hamster cells were obtained; reactions of MNNG and MNU with RNA revealed similar behavior. Methylation of either protein or RNA molecules is unlikely to be responsible for the cytotoxic effect of these agents.

2249 DISTRIBUTION OF N-[¹⁴C] METHYL-N-NITROSOUREA IN THE RAT AFTER SYSTEMIC ADMINISTRATION. (Ger.) Kleihues, P. (Max-Planck Inst., Cologne-Merheim, Germany) and K. Patzschke. *Z Krebsforsch* 75(3):193-200, 1971.

The distribution of N-¹⁴C-methyl-N-nitrosourea in the rat was investigated by total body autoradiography 2 min after i.v. administration of 100 mg/kg of the compound. The lowest level of activity was found in the bones and adipose tissue. The concentration of label was greater in muscle cells, especially in the tongue and neck. Highest activity was found in the liver, kidney, parotid gland, pancreas and spleen. The stomach and intestinal walls were also labeled. In the central nervous system, the cerebrum, the spinal cord, the cerebellum, the brain stem, and hypophysis were labeled in varying degrees; no activity was demonstrable in the subarachnoid space or in the basal cisterns.

2250 THE RESPONSE OF CHINESE HAMSTER CELLS TO N-METHYL-N'-NITRO-N-NITROSOGUANIDINE. (E.) Barranco, S. C. (U. Texas M.D. Anderson Hosp. Tumor Inst., Houston) and R. M. Humphrey. *Mutat Res* 11(4):421-429, 1971.

Synchronized Chinese hamster embryo cells in culture were treated with up to 5 µg/ml culture fluid of

N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) for 30 min; about 97% of treated cells failed to survive the minimal 0.5 µg/ml dose of MNNG when the treated cells were asynchronous. While cell survival was usually less than 1%, it was lowest (0.04%) in cells treated with MNNG during the G₁/S mitotic phase transition. When cells in the early S-phase were treated with MNNG it was found that the percentage of cells labeled with ³H-thymidine reached 92% by 3-4 hr after release of the synchronizing mitosis block, then fell to 31% by 7 hr and rose to 80% by 13 hr. Treatment with MNNG did not hinder the progression of cells from early S-phase to the G₂-phase. Treatment of cells in the G₂-phase with MNNG, however, did delay the progression of cells from this phase. When cells in mitosis were treated with MNNG it was found that untreated cells progressed out of mitosis and into G₁ in 1 hr with 0% mitotic index, the MNNG-treated cells however plateaued at 70% mitotic index for 2 hr.

- 2251 SOME CONTRIBUTIONS TO THE INFLUENCE OF THE AUTONOMIC NERVOUS SYSTEM ON THE EXPERIMENTAL INDUCTION OF CANCER OF THE STOMACH. (E.) Mizukami, T. (2nd Surg. Clin., Kanazawa U., Japan), O. Takamatsu and K. Miwa. *Neoplasma* 17(6):649-654, 1970.

Male rats were laparotomized and divided into 3 experimental groups; group I was vagotomized and given N-methyl-N'-nitro-N-nitrosoguanidine (NG, 50 mg/l water), group II was splanchnicotomized and given NG, and group III underwent no further surgery and was given NG. By 50 wk after treatment, 31% of controls had developed tumors of the glandular stomach, 59% of vagotomized rats had developed tumors and 22% of splanchnicotomized rats had developed tumors. More lethal cases of stomach cancer occurred in vagotomized rats than in splanchnicotomized rats. Surgical blockade of the vegetative nervous system, however, did not affect NG-induced stomach cancer incidence. It was suggested that vagotomy for peptic ulcer may entail an increased risk of developing cancer of the glandular stomach.

- 2252 STOMACH CANCER AND NEUROGENIC TUMORS INDUCED BY ORAL ADMINISTRATION OF METHYL-NITROSOBIURET (MNB) IN RATS. (Ger.) Druckrey, H. (Div. Prev. Med., Max-Planck-Inst., Freiburg, Germany), C. Landschütz, R. Preussmann and S. Ivankovic. *Z Krebsforsch* 75(3):229-239, 1971.

Chronic treatment with methyl-nitrosobiuret (MNB) of BD rats (5 mg/kg in the drinking water, stabilized with a phosphate buffer at pH 6, 5 times per wk for 378 days) induced gastric adenocarcinoma in 7 and brain tumors in 2 of 10 animals. Administration of 10 mg doses under similar conditions induced neurogenic malignancies in 10, glandular stomach tumors in 4 and adenocarcinoma of the pancreas in 1 of 16 rats. The average latency period was 490 and 400 days resp. for the 2 experimental groups. Single doses of 25, 50, 100, and 200

mg/kg of MNB (p.o. in oil suspension) induced squamous cell carcinoma of the forestomach in 5 and gastric adenocarcinoma in 1 of 15 rats, squamous cell carcinoma of the forestomach in 4 and adenocarcinoma of the pylorus in 1 of 10 rats, malignant tumors of the stomach in 3 and brain tumor in 1 of 8 rats, and forestomach tumors in 5 of 8 rats resp. The 11 rats given 400 mg/kg MNB developed a total of 16 malignant tumors of which neuroinomas or tumors of gastric locations were prevalent. The latency period decreased from 622 to 172 days with the increasing doses. Stomach and nervous system appeared to be the main targets for MNB carcinogenesis confirming the neurotropic effects of the urea group and the preferential tropism towards the glandular stomach.

- 2253 SKIN TUMORS IN MICE PAINTED WITH N-METHYL-N'-NITRO-N-NITROSOGUANIDINE AND N-ETHYL-NITRO-N-NITROSOGUANIDINE. (E.) Takayama, S. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), N. Kuwabara, Y. Azama and T. Sugimura. *J Nat Cancer Inst* 46(5):973-980, 1971.

Male strain ICR mice were treated with N-methyl-N'-nitro-N-nitrosoguanidine (MNG) or N-ethyl-N'-nitro-N-nitrosoguanidine (ENG) by topical application between the scapulae according to 1 of 5 protocols: group 1 consisted of 10 mice given a 0.15% solution of MNG for 5 months, group 2 consisted of 10 mice given a 0.3% solution of MNG for 5 months, group 3 consisted of 20 mice given a 0.5 solution of MNG for 5 months, group 4 consisted of 14 mice given a 0.5% solution for ENG for 5 months, and group 5 consisted of 15 mice given acetone solvent only for 5 months (controls). Squamous cell carcinomas developed in 4 of the mice in group 1, in 3 of 18 surviving mice in group 3 and in 5 mice in group 5. Groups 2 and 4 did not develop squamous cell carcinomas. Fibrosarcomas developed in 4 mice in group 1, in 6 mice in group 2, in 7 mice in group 3, in 1 mouse in group 4 and in none of the controls. In some tumor nodules squamous cell carcinoma and fibrosarcoma were found together; the nodules were designated "colliding malignant tumors". Colliding tumors were found in 1 mouse in group 1, in 2 mice in group 2, in 5 mice in group 3, in no mice in group 4 and in none of the controls.

- 2254 QUANTITATIVE ASPECTS OF THE REPAIR OF ALKYLATED DNA IN CULTURED MAMMALIAN CELLS. II. NON-SEMICONSERVATIVE DNA SYNTHESIS ('REPAIR SYNTHESIS') IN HeLa AND CHINESE HAMSTER CELLS FOLLOWING TREATMENT WITH ALKYLATING AGENTS. (E.) Roberts, J. J. (Roy. Cancer Hosp., London, England), J. N. Pascoe, B. A. Smith and A. R. Crathorn. *Chem Bio Interact* 3(1):49-68, 1971.

DNA "repair synthesis" in HeLa and Chinese hamster cells was followed by monitoring loss of labeled methyl and alkyl groups following treatment with various concentrations of N-methyl- and N-ethyl-N-nitro-N-nitrosoguanidine, N-methyl-N-nitrosourea,

thyl and ethyl methanesulphonate or mustard gas. The extent of repair synthesis was directly proportional to the amount of overall DNA alkylation in both cell lines and continued at an approximately equal rate up to 9 hr in hamster cells following alkylation and up to 12 hr in HeLa cells following alkylation with mustard gas. Repair synthesis occurred in both strands of DNA and was not inhibited by the substitution of 5-bromuracil for thymidine in DNA or by hydroxyurea. The ratio of specific activities of DNA synthesized by 'repair' and normal processes under several experimental conditions was similar.

55 CONTROLLING FACTORS IN URETHAN CARCINOGENESIS IN MICE: EFFECT OF ENZYME INDUCERS AND METABOLIC INHIBITORS. (E.) Yamamoto, R. S. Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md., J. H. Weisburger and E. K. Weisburger. *Cancer Res* 31(5):483-486, 1971.

Strain A/J mice were given a single i.p. injection of 1 mg urethan per g body wt following pretreatment with one of 5 microsomal enzyme inducers: chlordane, phenobarbital, β -naphthoflavone, phenothiazine or diethylaminoethyl diphenyl valerate (SKF-525A). Mice given urethan and no pretreatment developed 12 lung tumor nodules/mouse while mice pretreated with chlordane, phenobarbital or β -naphthoflavone developed 12, 10.3 and 13.3 nodules/mouse, resp. Phenothiazine and SKF-525A failed to reduce the number of lung tumor nodules developed. None of the microsomal enzyme inducers were carcinogenic to the lung by themselves. In mice given 3-methylcholanthrene, the incidence of ensuing tumors was reduced by a subsequent dose of urethan. Actinomycin D, puromycin, and cycloheximide failed to affect the incidence of tumors developed by mice treated with these agents and urethan.

56 GASTRIC TUMORS AND LUNG LESIONS IN THE RAT FOLLOWING THE INTRAGASTRIC OR INTRAPERITONEAL ADMINISTRATION OF N-(β -CHLOROETHYL)-N-NITROURETHAN. (E.) Schoental, R. (Med. Res. Council, Carshalton, Surrey, England) and J. P. M. *Cancer Res* 31(5):573-576, 1971.

Twenty-four weanling male rats were given 1 or 2 intragastric doses of N-(β -chloroethyl)-N-nitro-urethan (CENU) in amounts ranging from 2-50 mg/kg body wt. In those rats which were given a dose higher than 10 mg/kg death occurred within 2-14 days. Of 12 rats which survived longer than 1 yr after CENU treatment, 3 developed tumors in the fundular stomach, 1 developed a tumor of the forestomach and 1 developed a tumor of the esophagus. Stomach tumors were usually well-differentiated. Of 19 rats given 5 mg/kg CENU by i.p. injection, 10 survived for more than 6 months, and many died shortly after treatment.

57 ASBESTOS AND MESOTHELIOMAS. (E.) Godwin, M. C. (St. Mary of Nazareth Hosp., Chicago, Ill.) and J. Jagatic. *Environ Res* 3(5-6):391-416, 1970.

The role of asbestos exposure in the development of mesothelioma was investigated in 7 patients. Two female patients who died at 43 and 57 yr-of-age after 24 and 34 yr, resp., from the first exposure to asbestos had abdominal mesothelioma; the duration of exposure was 3 yr in the former and 13 yr in the latter case. Two male patients died of pleural mesothelioma 16 yr after a 16-yr exposure and 25 yr after a 3-yr exposure to asbestos. Two male patients died of abdominal mesothelioma 34 yr after a 13-yr exposure to asbestos. One female died with a pleural mesothelioma 41 yr after a 6-wk exposure to asbestos when she was 14 yr-of-age. Asbestos bodies were always found in the carcinomatous stroma, in the hilar nodes, in the lateral visceral pleural macrophages and lymphatics. Asbestos bodies, fragments, particles and dust seemed to be transported throughout the body and deposited mainly in the nodes, spleen and liver. Apparently carbon, silica and asbestos material were passed through hilar, mediastinal and clavicular nodes entering the circulatory system. Carbon and silica appeared to be localized in the liver and spleen. Asbestos bodies were also found in the intestinal mucosa. The dust found in the abdominal nodes and viscera may have been carried by the lymphatics. Mechanical irritation and chemical effects due to iron-containing compounds such as ferritin or hemosiderin were considered among the main malignancy-inducing factors in asbestosis.

2258 TUMORS IN MICE INDUCED BY AIR PARTICULATE MATTER FROM A PETROCHEMICAL INDUSTRIAL AREA. (E.) Rigdon, R. H. (U. Texas Med. Branch, Galveston) and J. Neal. *Texas Rep Biol Med* 29(1):109-123, 1971.

An air sampler was used to collect air pollutants from the area of a petrochemical plant in Texas City, Texas; air pollutants were collected 24 hr/day, 6 days/wk for 5 yr. A progressive increase in the amount of particulate matter in the air samples was seen during the period of collection. The concentrations of benzene-solubles and benzo(a)pyrene also increased in the air samples. Benzene-solubles and benzo(a)pyrene were extracted from the air samples and injected s.c. into strain CFW mice in amounts ranging from 1-20 mg. Benzene-solubles produced local fibrosarcomas in 40-61% of mice injected with 2.5-10.0 mg. Benzo(a)pyrene (0.025-2.0 mg) extracted from the air samples and injected into mice caused fibrosarcomas in 33-90% of mice. No tumors occurred in mice treated with benzene-solubles collected at areas other than the Texas City plant. Commercially-produced benzo(a)pyrene produced fewer tumors in treated mice than did the benzo(a)pyrene extracted from the air pollution samples, which may have been due to the presence of cocarcinogens in the air samples.

2259 THE PRESENCE OF RESINS AND 3,4-BENZOPYRENE IN THE ATMOSPHERE OF THE ELECTROLYSIS SHOPS IN ALUMINIUM PLANTS: THEIR ROLE IN CARCINOGENESIS. (Rus.) Konstantinov, V. G. (Sverdlovsk Med. Inst., U.S.S.R.) and A. I. Kuzminyuk. *Gig Sanit* 3:39-42, 1971.

Resinous compounds in the occupational environment of electrolysis operations within aluminium plants of Irkutsk varied from 8 to 2,400 mg/m³ and the levels of benzo(a)pyrene varied from 1 to 1,800 µg/m³ depending on the sampling area. Mortality from malignant neoplasia among male workers engaged in shops with self-burning anodes was 1.9 times higher for the whole group, 7.2 times higher among the 18-39-yr-old group and 1.6 times higher among above 40-yr-old workers than the urban area population over an 11 yr period (1956-1966). Mortality from lung, bronchial or pleural cancer was 1.7 times higher among the same workers (whole group), 8.3 times higher among the young and 1.6 times higher among the middle-aged group than among the urban population of the area. No significant excess in mortality from malignancy was observed among workers engaged in shops with burnt anodes who had no contact with coal pitch.

- 2260 A STUDY OF TOBACCO CARCINOGENESIS: XI. TUMOR INITIATORS, TUMOR ACCELERATORS, AND TUMOR PROMOTING ACTIVITY OF CONDENSATE FRACTIONS. (E.) Hoffmann, D. (Amer. Hlth. Found., New York, N. Y.) and E. L. Wynder. *Cancer* 27(4):848-864, 1971.

The BI subfraction of cigarette smoke condensate, a portion which contains polynuclear aromatic hydrocarbons, N- and O-heteroaromatic compounds, chlorinated insecticides and some of their pyrolysis products, esters, terpenes and quinones, was separated into 5 parts. One of these parts, BIh, comprised 0.09% of total cigarette "tar" and 15% of the subfraction BI; BIh contained 48% of the benzo(a)pyrene content of subfraction BI. The BIh portion was chromatographed into 80 subfractions and each subfraction was tested for tumorigenicity by administering it topically to strain Ha/ICR mice. BIh subfractions 56-66 were highly tumorigenic; the tumor incidence among mice given these fractions ranged from 17% to more than 80%. Fractions 70-80 were also effective as tumor initiators and produced tumor incidences of 35-65%. While fractions 56-66 contained no known carcinogens, other fractions of BIh contained alkylated fluoranthenes, cyclophenanthrenes and chrysene. It was noted that only the acidic portions of tobacco "tar" fractions showed appreciable tumor-promoting efficacy.

- 2261 INFLUENCE OF CIGARETTE SMOKE ON GUINEA PIGS: EFFECT ON PULMONARY CELLS AND SERUM ANTITRYPSIN LEVELS. (E.) Flint, G. L. (VA Hosp., Salt Lake City, Utah), K. W. Maxwell and A. D. Renzetti, Jr. *Arch Environ Health* 22(3):366-369, 1971.

Male guinea pigs were exposed to the smoke of 40 cigarettes/day for 2 wk and to the smoke of 20 cigarettes/day for 8 wk thereafter, and the number and type of cells recoverable from the lungs were noted together with the antitrypsin contents of serum. More total cells were recoverable from the lungs of animals exposed to smoke than from animals not exposed to smoke; the overall mean number of cells recovered from the lungs of treated guinea

pigs was 11.7×10^6 and the overall mean number of cells recovered from the lungs of controls was 8.1×10^6 . Fifty percent of cells recovered from the lungs of exposed animals were polymorphonuclear leukocytes while 24% of cells recovered from control lungs were polymorphonuclear leukocytes. No changes were seen in the levels of serum antitrypsin levels during the 10 wk experimental period in exposed animals.

- 2262 TEMPORAL CHANGES IN DNA AND RNA SYNTHESIS IN THE REGENERATING LIVER OF HYDROCORTISONE-TREATED RATS. (E.) Rizzo, A. J. (McGill U. Cancer Res. Unit, Montreal, Quebec, Canada), P. Heilpern and T. E. Webb. *Cancer Res* 31(6):876-881, 1971.

Male rats were partially hepatectomized 19 hr prior to administration of 50 mg/kg hydrocortisone. It was found that hydrocortisone inhibited a rise in DNA synthesis in the regenerating liver. In non-hepatectomized rats not given hydrocortisone, DNA synthesis (measured by the uptake of ³H-thymidine by liver cells in cpm/µg deoxyadenosine) rose from 5-21 cpm/µg during 20-26 hr after hepatectomy; however, in hydrocortisone-treated rats, there was no appreciable increase in DNA synthesis 20-32 hr after hepatectomy. Between 32 and 36 hr, as DNA synthesis in untreated hepatectomized rats declined, DNA synthesis in hydrocortisone-treated animals increased from 5-42 cpm/µg. Further, the rate of ribosome formation in hydrocortisone-treated rats increased by 150-200% over controls by 26 hr postoperative; by 32 hr postoperative, the increase in ribosome formation in hydrocortisone-treated rats was 120-200% over controls. Most of the increase in ribosome formation in treated rats was thought to be due to increased transport of ribosomal subunits to the cytoplasm.

- 2263 CARCINOGENICITY OF INDUSTRIAL CHEMICALS: PROPYLENE IMINE AND PROPANE SULFONE. Ulland, B. (Bionetics Res. Labs., Inc., Kensington, Md.), M. Finkelstein, E. K. Weisburger, J. M. R. and J. H. Weisburger. *Nature* 230(5294):460-461, 1971.

Groups of 26 rats were given p.o. doses of either 10 mg/kg propylene imine for 28 wk or 56 or 28 mg/kg propane sulfone for 32 wk. Of the 52 rats given 20 mg/kg propylene imine 28 developed tumors and of the 52 rats given 10 mg/kg propylene imine 45 developed tumors. Tumors in the propylene imine group included 30 breast tumors among females, 1 gliomas, 9 ear duct tumors, 10 leukemias, 4 intestinal tumors and 10 "miscellaneous" tumors. Propane sulfone at both dose levels gave rise chiefly to gliomas (56 gliomas developing in the 52 rats treated). Breast tumors, ear duct tumors, leukemias, intestinal tumors and miscellaneous tumors also developed in rats given propane sulfone, and intestinal tumors were more common in the propane sulfone group than in the propylene imine group.

- 4 A STUDY OF PRECURSOR ILLNESS IN LUNG CANCER PATIENTS. (E.) Stavrakys, K. M. (Community Med., U. Western Ontario, Canada). *Chronic Dis* 23(10-11):691-705, 1971.
- The histories of 526 Canadian veterans who had died of lung cancer were matched for age, occupation, residence and cigarette smoking habits with an equal number of controls without lung cancer. Illness patterns emerging prior to the onset of cancer were compared. No significant pattern, however, emerged in the cancer group which would have permitted the prediction of susceptibility to lung cancer. Minor differences in illness patterns were found between cancer cases and non-cancer cases that appeared to be related to smoking habits. It was found that cancer patients smoked more intensely than non-cancer patients who smoked the same number of cigarettes (smoking "intensity" was measured by measuring amount of smoking and duration of each cigarette).
- 5 CARCINOMAS OF THE NOSE IN RATS AFTER CHRONIC INHALATION OF METHYL-BUTYLNITROSAMINE AT 5 ppm. (Ger.) Druckrey, H. (Max-Planck Inst., Marburg, Germany) and Ch. Landschütz. *Z Krebsforsch* 73(3):221-224, 1971.
- 6 POLYCYCLIC AROMATIC HYDROCARBONS: COVALENT BINDING TO DNA AND EFFECTS ON TEMPLATE FUNCTION. (E.) Chan, E. W. (Cancer Res. Lab., U. Western Ontario, London, Canada) and J. K. Ball. *Chem Phys Acta* 238(1):46-59, 1971.
- 7 AFLATOXIN BIOSYNTHESIS IN *ASPERGILLUS PARASITICUS*: EFFECT OF METHIONINE ANALOGS. (E.) Roy, R. W. (Northern Reg. Lab., Peoria, Ill.) and Siegler. *Canad J Microbiol* 17(5):569-574, 1971.
- 8 EXCRETION OF NICKEL COMPOUNDS BY THE RAT: BLOOD AND URINE LEVELS. (E.) Chen, J. K. (Inst. Chem. Biol., U. San Francisco, Calif.), C. Haro and A. Furst. *Wasmann J Biol* 29(1):1-15, 1971.

- 2269 CARCINOGENIC NITROGEN COMPOUNDS: LXIX. SYNTHESIS OF POLYCYCLIC THIAZOLES FROM 4,5-DIHYDRO-2-METHYLBENZOTHAZOL-7(6H)-ONE. (E.) Buu-Hoi, N. P. (Inst. Chem. Natural Substances, C.N.R.S., Gif-sur-Yvette, France), A. Croisy, P. Jacquignon and A. Martani. *J Chem Soc* 1971(6):1109-1111, 1971.
- 2270 TRANSFORMATION OF KIDNEY CELLS IN CULTURE BY CHEMICAL CARCINOGENS: I. TRANSFORMATION OF RAT KIDNEY CELLS IN CULTURE WITH 4-NITROQUINOLINE-1-OXIDE. (Jap.) Ochiai, M. (Dept. Urol., Sch. Med., Showa U., Japan). *Jap J Urol Assoc* 62(1):1-12, 1971.
- 2271 THE RELEVANCE OF CHEMICO-BIOLOGICAL INTERACTIONS FOR THE TOXIC AND CARCINOGENIC EFFECTS OF AROMATIC AMINES: II. DISTRIBUTION OF RADIOACTIVITY AFTER THE ADMINISTRATION OF THE TRITIUM LABELED CARCINOGEN TRANS-4-DIMETHYLAMINOSTILBENE AND THE NONCARCINOGENIC CIS-4-DIMETHYLAMINOSTILBENE AND 4-DIMETHYLAMINOBIENZYL IN THE RAT. (Ger.) Rjosk, H. K. (Max-Planck-Inst., Munich, Germany) and H.-G. Neumann. *Z Krebsforsch* 75(3):209-220, 1971.
- 2272 PSEUDOWASTING SYNDROME AND CARCINOGENESIS AFTER 20-METHYLCHOLANTHRENE INJECTED INTO NEWBORN AND YOUNG ADULT MICE. EFFECTS OF MYCOBACTERIUM CALMETTE-GUERIN (BCG). (Ger.) Zschiesche, W. (Central Inst. Microbiol., Exp. Therap., German Acad. Sci., Berlin, Germany) and W.-D. Schulz. *Z Krebsforsch* 75(4):277-287, 1971.
- 2273 CHROMOSOME STUDY IN A CASE OF GRANULOCYTIC LEUKAEMIA WITH 'PELGERISATION' 7 YEARS AFTER BENZENE PANCYTOPENIA. (E.) Sellyei, M. (Robert-Károly Hosp., Budapest, Hungary) and E. Kelemen. *Europ J Cancer* 7(1):83-85, 1971.

See also:

- * (Rev): 2146, 2149, 2151, 2152, 2154, 2168, 2171, 2176
- * (Phys): 2294
- * (Immun): 2423, 2424, 2426, 2434, 2435, 2440
- * (Path): 2470, 2478
- * (Epid-Biom): 2490

- 2274 PROTEASE ACTIVITY CHANGES IN RABBIT LUNG
MACROPHAGES, SPLEEN CELLS AND POLYMOR-
PHONUCLEAR LEUCOCYTES AFTER WHOLE-BODY X-IRRADIATION.
(E.) Kotulova, D. (Fac. Med., Comenius U., Bratis-
lava, Czechoslovakia) and J. Stefanovic. *Folia*
Biol (Praha) 17(1):26-32, 1971.

Intracellular protease activity (at pH 3.2 and pH 2) in polymorphonuclear leukocytes, spleen cell sus-
pensions (70% lymphocytes) and alveolar macrophages
was investigated in 84 rabbits 1 hr and 1, 2, 3, 6,
10 and 20 days after exposure to whole-body irradi-
ation (500 R). The proteolytic activity of poly-
morphonuclear leukocytes increased during the 1st
few hr, decreased on the 6th day and returned to
normal values by the 10th day following exposure;
no further changes in activity were recorded at pH
2 but a significant increase in activity was
observed at pH 3.5 20 days after exposure. Lung
macrophages elicited a 95% increase in protease
activity the 6th through the 10th day; protease
returned to normal values on the 20th day of the
experiment at both pH levels. The proteolytic
activity of spleen cell extracts determined at pH
3.5 displayed a biphasic course: an 80% increase
occurred on the 1st day and a second peak was
recorded on the 10th day with a decrease to almost
normal values on the 20th day following irradiation.
The increased proteolytic activities seemed to be
due to enzyme participation in the lysis of protein
from injured cells.

- 2275 BONE MARROW, SPLEEN, AND THYMUS REGENERA-
TION PATTERNS IN MICE AFTER WHOLE-BODY
IRRADIATION. (E.) Takada, A. (Roswell Park Mem.
Inst., Springville, N. Y.), Y. Takada, U. Kim and
J. L. Ambrus. *Radiat Res* 45(3):522-535, 1971.

Male mice of the CBA/St strain were exposed to 400 r
of whole-body X-irradiation; some mice had been
thymectomized prior to irradiation. Spleen weight
in irradiated mice decreased from 77 mg at irradiation
to a low of 30 mg on day 5 postirradiation, there-
after recovering rapidly to attain a maximum of 180
mg on day 18. Injection of 5×10^6 bone marrow cells
following irradiation induced an earlier recovery of
spleen weight after irradiation, and shielding the
right femur during irradiation had a similar effect.
Following irradiation, the thymus showed a biphasic
pattern of weight change. Incorporation of ^{59}Fe by
spleen and bone marrow declined following irradiation
until day 2 and then increased until days 6-7
after which label incorporation declined again
before making a rapid recovery between days 11 and
18 postirradiation. Incorporation of $^{125}\text{IUdR}$ in
spleen, bone marrow and thymus showed a similar pat-
tern of decline and recovery following irradiation.
Injection of bone marrow cells following irradiation
produced an earlier recovery of ^{59}Fe and $^{125}\text{IUdR}$
incorporation; in animals given bone marrow cells,
incorporation peaked on day 10 postirradiation.
Shielding of the femur during irradiation similarly
produced more rapid recover of ^{59}Fe and $^{125}\text{IUdR}$
incorporation; however, cells migrating from bone
marrow to spleen in the protected mice commenced
synthesis of hemoglobin immediately while injected

bone marrow cells did not initiate division or hem-
oglobin synthesis for as long as 2 days after
irradiation.

- 2276 A QUANTITATIVE ANALYSIS OF BONE MARROW
CELL POPULATIONS IN IRRADIATED AND NON-
IRRADIATED MICE TREATED WITH 19S ALPHA-2 GLOBULIN
($\alpha_2\text{-MG}$). (E.) Sontag, J. M. (Weizmann Inst. Sci.
Rehovot, Israel), N. Trainin and I. Berenblum.
Radiat Res 45(3):499-510, 1971.

Mice of strain C57BL/6 were treated with 4 i.v.
injections of 0.50 mg of 19S α_2 -globulin prior to
exposure to 680 r of X-irradiation. Cell volume
distribution was measured in bone marrow of treated
mice with a device similar to a Coulter counter.
The volume distribution of cells from normal
unirradiated mice fell into 3 categories: cells
with volumes of $10\text{-}107 \mu^3$ (group 1), cells with
volumes of $108\text{-}214 \mu^3$ (group 2), and cells with
volumes of $215\text{-}425 \mu^3$ (group 3). In unirradiated
mice treated with α_2 -globulin, the number of group
1 cells rose after 6 hr of treatment from 10×10^6
to 13×10^6 , thereafter falling to 5×10^6 on day
posttreatment. At the same time, cells in group
dropped from 8×10^6 after 1 hr of treatment, to
 $\times 10^6$ by 12 hr and recovered by day 5. In mice
treated with α_2 -globulin and given irradiation,
(and in untreated irradiated mice), cells in group
1 rose from about 10×10^6 at 1 hr after treatment
to about $19\text{-}21 \times 10^6$ at 24 hr after treatment,
falling to initial values by day 8. Groups 2 and
declined markedly following irradiation. Treatme-
with α_2 -globulin stimulated recovery of group 3.

- 2277 FACTORS REGULATING THE PROLIFERATION AND
MIGRATION OF HEMATOPOIETIC STEM CELLS.
(E.) Fried, W. (Sec. Hematology, Div. Med., Rush
Presbyterian St. Luke's Med. Ctr., Chicago, Ill.)
J Lab Clin Med 77(2):239-246, 1971.

Female mice of the CF₁ strain were exposed to X-ir-
radiation at a dose rate of 30-50 rads/min with 1
leg shielded from X-rays; numbers of hematopoietic
stem cells (HSC) in the organs of the animals were
determined by observing the number of colony form-
ing units in selected tissues. In all tissues
studied, the number of colony forming units was
greater in irradiated mice than in unirradiated
mice; a dose of 300 rads produced 20 colony form-
ing units in spleens of irradiated mice, while unirra-
diated mice spleens showed less than 1 unit. Colon-
forming units were not significantly more abundant
in the shielded legs of irradiated mice than in 1
of unirradiated mice. Irradiated mice were expos-
ed to an additional 200 rads and previously unexposed
control mice also received 200 rads X-rays; the num-
ber of colony forming units in the bone marrow of
both irradiated mice and control mice declined to
10% of normal. However, by 24 hr after the 200 r
dose, the number of colony forming units in the
marrow of mice given the priming irradiation was
twice as much as that of mice not exposed to prim-
ing irradiation. The percentage of colony forming un-

surviving vinblastine treatment in the shielded marrow and in marrow of unirradiated mice was not significantly different; however, the percentage of colony forming units surviving vinblastine treatment in the unshielded marrow was less than half that surviving in the marrow of unirradiated mice or in the shielded marrow of irradiated mice.

2278 A CYTOLOGICAL STUDY OF BONE MARROW AND PERIPHERAL BLOOD OF IRRADIATED AND NON-IRRADIATED MICE TREATED WITH 19S ALPHA-2 GLOBULIN (α_2 -MG). (E.) Sontag, J. M. (Weizmann Inst. Sci., Rehovot, Israel), I. Berenblum and N. Trainin. *Radiat Res* 45(3):511-521, 1971.

Female strain C57BL/6 mice were exposed 4 times to 170 r of X-irradiation and treated subsequently with an i.v. injection of 0.50 mg 19S α_2 -globulin; the effects of treatment on populations of cells in bone marrow and peripheral blood were observed. In irradiated and unirradiated mice given α_2 -globulin, granulocytosis followed treatment; in these groups, granuloid cells increased in bone marrow until 3 days after treatment, thereafter dropping to sub-normal levels before returning to normal levels on day 10. Lymphocytes and lymphocyte-like cells in bone marrow of mice given α_2 -globulin but no irradiation increased following treatment; enhanced production of granulocytes followed lymphocyte increase in these experimental groups. Lymphocyte and granuloid cells in bone marrow of irradiated mice given α_2 -globulin recovered normal levels more quickly than did cells of mice not given α_2 -globulin. In the peripheral blood, leukocyte counts of mice given irradiation fell following irradiation, and recovered only gradually; by 21 days after irradiation, counts of leukocytes in this group were $1.5 \times 10^3/\text{mm}^3$. In irradiated mice given α_2 -globulin, however, leukocyte counts recovered more quickly; at 21 days after irradiation leukocyte counts in this group reached $4 \times 10^3/\text{mm}^3$.

2279 AUTORADIOGRAPHIC STUDIES ON ^3H -THYMIDINE INCORPORATION IN THE LIVER AND KIDNEYS OF IRRADIATED MICE. (E.) Unger, E. ("Frederic Joliot-Curie" Natl. Res. Inst. Radiobiol. Radiohygiene, Budapest, Hungary) and J. Gidali. *Strahlentherapie* 41(3):354-357, 1971.

Mice were exposed to 200, 450 or 700 r of X-irradiation and the incorporation of ^3H -thymidine into liver and renal tubulus cells of irradiated mice was observed at various times after irradiation. Tritiated thymidine uptake, expressed as a percentage of uptake in unirradiated mice, decreased in liver and kidney cells until 6 days postirradiation. No clear correlation was seen between increased dose of irradiation and increased or decreased thymidine labeling index. In liver cells given 450 r, the percentage of labeled cells dropped from 37% of control values immediately after irradiation to 10% by 24 hr postirradiation; at 72 hr postirradiation, the labeling index was still 10% of control. However, by 6 days postirradiation, the labeling index amounted

to 17% of control values; at 9 days postirradiation, the percentage of cells incorporating ^3H -thymidine was 60% of control values. Liver and kidney cells of irradiated mice never returned to normal.

2280 CHROMOSOMAL ABNORMALITIES IN LYMPHOCYTES OF CHILDREN AND BABY RABBITS BORN FROM MOTHERS TREATED BY X-IRRADIATION BEFORE PREGNANCY: A TRANSPLACENTARY PLASMATIC CHROMOSOME-DAMAGED FACTOR? (E.) Goyanes-Villaescusa, V. (Med. Santiago de Compostela, Spain). *Blut* 22(2):93-96, 1971.

Karyotype studies were performed on the offspring of 6 women given non-pelvic radiotherapy in amounts ranging from 4,000-12,000 r, 2-8 months prior to pregnancy and in the offspring of 3 rabbits given whole-body X-irradiation (120 r/day) a week before breeding. All children showed a high frequency of unstable chromosome aberrations (e.g., 13.50% incidence) compared to the 4 children of unirradiated mothers who showed a 2.5% incidence of unstable chromosomal aberrations. The frequency of gaps, breaks, and dicentric in the children of irradiated mothers was 10, 2.65, and 0.65%, resp., while the frequency of these 3 aberrations in the children of unirradiated mothers was 1.9, 0.6, and 0%, resp. The frequency of unstable aberrations in the irradiated female rabbits and in unirradiated rabbits was 20 and 3%, resp. It was thought that a lymphocyte chromosome-breaking factor was induced in women and in female rabbits by irradiation, and that this factor passed through the placenta producing aberrations in offspring.

2281 INCIDENCE OF DOMINANT LETHAL MUTATIONS AFTER X-IRRADIATION OF SPERMATOZOA OF MICE AND RATS. (E.) Gilliavod, N. (Nuclear Energy Study Ctr., Mol, Belgium) and A. Leonard. *Strahlentherapie* 41(3):351-353, 1971.

Male BALB/c mice and male rats were exposed to 400 r of whole-body X-irradiation and mated for a period of 7 days with 3 virgin females immediately thereafter. On day 17, after the initiation of the mating period, females were killed and dissected and the numbers of corpora lutea and living and dead embryos were noted. The incidence of dominant lethality induced in spermatozoa by the irradiation was found to be approximately 50% higher in rats than in mice.

2282 CELL POPULATION KINETICS IN ACUTE INTESTINAL RADIATION DEATH. (E.) Okumura, Y. (Aichi Cancer Ctr. Res. Inst., Nagoya, Japan) and T. Matsuzawa. *Strahlentherapie* 41(3):358-362, 1971.

The cell renewal system in which cells produced in the crypts of the small intestine migrate to the villi was used as a model for the study of cell population kinetics in acute radiation death; the crypt cells were designated the "proliferative" compartment in the model and the villi cells the

"functional" compartment. Radiation death was induced in CFW mice by 300 r of X-irradiation. After irradiation, the cell number in the proliferative compartment decreased exponentially. Change in the cell number in the functional compartment was expressed in terms of the numbers of influx and efflux cells, and the decline in the cell number in the proliferative compartment produced a subsequent depletion in the functional compartment. The cell renewal system model was thought to give an adequate picture of the mechanism of cell denudation following radiation.

2283 CHROMOSOME DAMAGE IN THYROID CELLS OF ADULTS IRRADIATED WITH X-RAYS IN INFANCY.

(E.) Doida, Y. (U. Rochester Sch. Med. Dent., N. Y.), C. Hoke and L. H. Hempelmann. *Radiat Res* 45(3):645-656, 1971.

Cells from neoplastic and nonneoplastic thyroids of 4 humans given (in 2 cases) 728 and 468 r of X-irradiation in infancy together with 50 μC ^{131}I were examined for chromosomal aberrations. These patients were aged from 28-37-yr-old. Controls consisted of patients given ^{131}I but no irradiation and subjects given neither ^{131}I nor irradiation. Aneuploid metaphases were more common in thyroid cells from the X-irradiated group than in controls; the percentages of aneuploid metaphases in irradiated patients ranged from 6.4-20.8%, while percentages of aneuploid metaphases from unirradiated ^{131}I -treated patients ranged from 0-17.8%, and percentages of aneuploid metaphases from patients given neither X-irradiation nor ^{131}I ranged from 0-3.8% (0% in 5 of 7 patients in this group). Aneuploid metaphases were in all groups more common in normal cells than in neoplastic cells. In both neoplastic and normal cells the frequency of unstable aberrations was 3.5% in irradiated patients; this frequency was 10 times higher than the frequencies of unstable aberrations in either of the control groups. The frequency of stable aberrations in X-irradiated patients was 32.6% in normal thyroid cells and 22.6% in neoplastic cells. In controls, the frequency of stable aberrations in normal and neoplastic cells never exceeded 2%.

2284 EFFECT OF INTERNAL EXPOSURE BY ^{90}Sr AND ^{131}I ON RESPIRATORY $^{14}\text{CO}_2$ PATTERNS FOLLOWING ^{14}C -GLUCOSE ADMINISTRATION IN MICE. (E.) Matsuoka, O. (Natl. Inst. Radiol. Sci., Chiba, Japan), E. Muramatsu and M. Kashima. *J Radiat Res* 11(3-4):157-165, 1970.

Male hybrid mice of strain CF1 and RF were given 2 $\mu\text{C/g}$ body weight of ^{90}Sr or 5 $\mu\text{C/capita}$ ^{131}I , and the effects of this irradiation on the respiratory $^{14}\text{CO}_2$ patterns were compared using ^{14}C -glucose. Parameters compared in ^{90}Sr - and ^{131}I -irradiated mice included the time elapsing between irradiation to maximum specific exhalation of $^{14}\text{CO}_2$ and CO_2 (peak time) and the maximum exhalation activity at the peak time. In unirradiated mice, the value for specific activity of exhaled $^{14}\text{CO}_2$ had a maximum height of

1525 cpm/ CO_2 mM and a peak time of 26.1 min. In mice given ^{90}Sr irradiation, the maximum height did not differ significantly from that seen in unirradiated mice, but the peak time was decreased to 17.5-20 min. In mice given ^{131}I , the peak time for specific activity of exhaled $^{14}\text{CO}_2$ was not significantly different from that seen in unirradiated mice, but the maximum value for specific $^{14}\text{CO}_2$ exhalation activity was increased to 2039-2051 cpm/ CO_2 mM. L-thyroxine and insulin produced a stimulatory effect; maximum height of specific $^{14}\text{CO}_2$ activity was increased and peak time was decreased in irradiated mice given these agents. 5-Hydroxytryptamine and carbon tetrachloride inhibited the specific activity of $^{14}\text{CO}_2$ in irradiated mice.

2285 PATHOLOGIC EFFECTS OF DIFFERENT DOSES OF RADIOSTRONTIUM IN MICE: DEVELOPMENT AND INCIDENCE OF LEUKAEMIA. (E.) Nilsson, A. (Res. Inst. of Natl. Defense, Sundbyberg, Sweden). *Acta Radiol* 10(1):115-128, 1971.

The incidence of leukemia and related conditions observed among 1,430 strain CBA mice which were injected i.p. with doses of $^{90}\text{Sr}(\text{NO}_3)_2$ ranging from 0.2-1.6 $\mu\text{C/g}$ body wt. Mice were killed 7, 14, 30 days after treatment with ^{90}Sr and their blood and selected organs were examined for leukemia. In the treated rats, 991 died before being killed for examination. A total of 98 cases of leukemia were discovered in the ^{90}Sr -irradiated mice. The highest incidence of leukemia developed among mice given 1.6 $\mu\text{C/g}$ ^{90}Sr (28.0% incidence) and the lowest incidence developed among mice given 0.2 $\mu\text{C/g}$ ^{90}Sr (1.7% incidence). Of the 98 cases of leukemia developed by the irradiated mice, 97 were thought to have arisen from the lymphatic cells; there were 60 cases of marrow lymphomas and 21 thymic lymphomas. There were 16 cases of "generalized lymphoma" and 1 case each of myeloid and chronic lymphocytic leukemia.

2286 DETECTION OF A LUNG TUMOR AGENT IN BALB/c/Cb/Se IRRADIATED MICE. (E.) Squartini, F. (Inst. Pathological Anat. and Histology, U. Pisa, Italy) and G. B. Bolis. *Lav Ann Anat* Perugia 30(3):125-128, 1970.

Castrated male and intact female mice of BALB/c/Se strain, the offspring of sibling mates, were exposed to 500 r whole-body X-irradiation; 30 days thereafter, the mice were implanted with the parenchyma of newborn donors. Of 29 irradiated plant recipients, 8 developed thymic leukemia; none of the 30 unirradiated recipients developed leukemia. Five of the irradiated recipients developed alveolar adenomas in the lung grafts; no adenomas developed in the lung grafts of nonirradiated mice.

2287 QUANTITATIVE CHANGES OF ACID PHOSPHATASE IN THE HYPOTHALAMUS, PITUITARY, ADIPOSE TISSUE AND THYROID OF MICE (*Mus musculus* L.) EXPOSED TO

ARGE, SINGLE DOSES OF UV OR X-RAYS, TAKING INTO ACCOUNT THE CIRCADIAN RHYTHM. (E.) Surowiak, J. Dept. Anim. Physiol., Jagiellonian U., Cracow, Poland). *Folia Biol* 17(2):105-140, 1969.

Male and female mice were subjected to either a single dose of 1800 r of X-irradiation at 11 a.m. or a single dose of UV irradiation (254-405 nm) between 10 and 11 a.m. and the effect of these treatments on the circadian rhythm of acid phosphatase in various organs was noted. In the hypothalamus of unirradiated male animals the maximum acid phosphatase activity was seen at 6 p.m. and the minimum at midnight; in males given X-irradiation, the minimum acid phosphatase activity was seen at noon and at 6 p.m. UV produced a circadian pattern of acid phosphatase in the hypothalamus similar to that seen in unirradiated animals. In females given X-irradiation, the maximum levels of acid phosphatase in the hypothalamus were seen at 6 p.m. and midnight and the minimum values were seen at noon and 6 a.m. UV irradiation of females did not alter the normal acid phosphatase pattern until 12 hr after treatment; thereafter enzyme levels declined until 24 hr after treatment. Other organs and glands tested included the hypophysis, adrenal and thyroid. In all test targets, X-rays caused changes in acid phosphatase activity during the first 12-18 hr after treatment; enzyme levels usually returned to normal by 24 hr after treatment. In the other organs, as in the hypothalamus, UV and X-irradiation increased acid phosphatase in males and decreased acid phosphatase in females.

88 SUNLIGHT EXPOSURE AND RISK OF DEVELOPING CUTANEOUS AND ORAL SQUAMOUS CELL CARCINOMAS IN WHITE CATS. (E.) Dorn, C. R. (Sch. Vet. Med., U. Missouri, Columbia), D. O. N. Taylor and R. Schneider. *Nat Cancer Inst* 46(5):1073-1078, 1971.

The incidence of squamous cell carcinoma among domestic cats in Alameda County, California in 1965 was investigated. It was found that the annual incidence rates for carcinoma in this area were 26.9 cutaneous cases/100,000 cats and 9.0 oral cases/100,000 cats, suggesting that skin protected from exposure to sunlight is less apt to develop squamous carcinoma than skin which is regularly exposed to sunlight. Male and female cats, and spayed and intact cats did not show differing risks of developing squamous cell carcinoma. White cats had a risk of developing cutaneous squamous cell carcinoma 13 times greater than cats of other colors, but a similar difference in risk for white and non-white cats was not found for oral carcinoma. A low rate of incidence of cutaneous carcinoma was found for Siamese cats, the result perhaps of their non-white hair coat. Eighty-seven of the 149 squamous cell carcinoma cases in cats involved the ears and nose, areas which have comparatively little hair.

89 HOST RESISTANCE AND RADIATION RESPONSE OF SYNGENEIC MOUSE LYMPHOMA CELLS. (E.) Suyama, Y. (Coll. Med. Sci., U. Minnesota, Minneapolis). *J Nat Cancer Inst* 46(5):963-971, 1971.

Strain C57BL mice were exposed to 400 r of whole-body X-irradiation several hours to 1 day prior to challenge with cells from an LSA ascites lymphoma. Tumor takes in irradiated and unirradiated animals were compared. Most tumor takes represented the outgrowth of a single cell. In unirradiated mice, tumor takes following challenge ranged from 5/20 to 17/20, while in irradiated animals tumor takes ranged from 12/26 to 10/20. In a related experiment, irradiated and unirradiated mice were challenged with lymphoma cells killed by *in vitro* irradiation with 6000-9000 r. Prolongation of median survival time and a dose-dependent decrease in tumor takes were seen in unirradiated mice given X-ray killed lymphoma cells. Addition of numbers of killed cells to viable cells in the tumor cell challenge did not affect the incidence of tumor takes.

2290 THE EFFECTS OF X-RAYS ON THE SYNTHESIS OF DNA, RNA, AND PROTEINS IN SYNCHRONIZED CHINESE HAMSTER CELLS. (E.) Bacchetti, S. (Argonne Natl. Lab., Ill.) and W. K. Sinclair. *Radiat Res* 45(3):598-612, 1971.

Synchronized cultures of Chinese hamster cells were exposed to X-irradiation with a single absorbed dose of 710 rads, and the effect of the irradiation on RNA, DNA and protein synthesis in the cells was observed. Cells irradiated in the G₁ phase were slightly stimulated to enter the S phase but DNA synthesis was normal. Irradiation of cells in the S phase caused an initial decrease in DNA synthesis followed by an increase; in S phase cells the period of DNA synthesis was prolonged. RNA synthesis in irradiated cells increased as cells entered S phase and was maximal during the period of DNA replication; RNA synthesis decreased during G₂. Protein synthesis was stimulated to a greater degree by X-irradiation than either RNA or DNA synthesis. When cells were treated with 50 µg/ml cycloheximide for 3 hr after irradiation in the G₁ and G₂ phases, loss of colony-forming ability and inhibition of nucleic acid and protein synthesis associated with irradiation were somewhat mitigated.

2291 TOXICITY OF TRITIATED THYMIDINE IN P388F LYMPHOMA CELLS: II. EFFECTS ON DNA MOLECULAR WEIGHT. (E.) Peterson, A. R. (Christie Hosp., Manchester, England) and B. W. Fox. *Int J Radiat Biol* 19(3):237-246, 1971.

Mouse lymphoma cells of line P388F were labeled with 10 µCi/ml of tritiated thymidine (³H-TdR) for 30 min at 37°C and the effects of the incorporated tritium label on the molecular weight of DNA synthesized by the lymphoma cells were observed. It was found that the average molecular weight of DNA in the lymphoma cells was inversely related to the level of specific activity of label uptake by cells and to cell survival. At low levels of tritium incorporation, the medium-sized DNA component with an average molecular weight of about 2.5 x 10⁸ daltons was converted into the high molecular weight DNA fraction having an average molecular weight of about 10⁹ daltons. Supralethal

levels of tritium uptake or incubation of the labeled cells at 4°C reduced the average molecular weight of the larger DNA fraction. The decline in the molecular weight of DNA appeared to be produced by excess tritium incorporation due to strand breakage induced by the label.

2292 EFFECTS OF COBALT-60 GAMMA RAYS ON
LYSOZYME IN AQUEOUS SOLUTION. (E.)

Yamamoto, K. (Fac. Sci., Osaka U., Japan). *J Radiat Res (Tokyo)* 11(2):85-91, 1970.

Egg-white lysozyme was exposed to γ -irradiation produced by ^{60}Co in doses ranging from 5.4×10^4 to 1.4×10^6 r. The smaller dose left 95% of lysozyme activity intact, whereas the larger dose left 31% of lysozyme activity intact. In the lysozyme preparation given the smaller dose of γ -irradiation, no significant change is observed in amino acid composition or in amide-nitrogen content. No N-terminal amino acids other than lysine were detected. Polymerized lysozyme was found in irradiated lysozymes in addition to intact lysozyme.

2293 EFFECTS OF X-IRRADIATION ON ^{14}C -PYRUVATE
METABOLISM IN RAT THYMOCYTES. (E.) Araki,
K. (Tokyo Women's Med. Coll., Japan), S. Taguchi, H.
Ohya and T. Yamada. *J Radiat Res (Tokyo)* 11(2):
79-84, 1970.

The effect of X-irradiation on the label distribution of citric acid cycle intermediates from U- ^{14}C -pyruvate was studied in rat thymocyte cells. The glycogen content of irradiated thymocytes was considerably lower than control levels after a 2 hr incubation; malate accumulation was 10-50% above control levels and was dose-dependent (1-8 kR). Chromatographic patterns of citric acid cycle intermediates labeled with ^{14}C -pyruvate were essentially the same between the unirradiated control and irradiated cells. Label incorporation into glucose was decreased by 8 kR irradiation to 28% of control values. These findings indicate that the previously reported increased labeling of citric acid cycle intermediates derived from ^{14}C -glucose after irradiation was due to enhanced substrate flow through glycolysis rather than to stimulation of the citric acid cycle.

2294 THE ROLE OF CHEMICAL CARCINOGENS AND
IONIZING RADIATION IN THE DEVELOPMENT OF
COLONIC ADENOCARCINOMA. (Rus.) Zapol'skaya, N. A. (no affil),
Fedorova, L. N. Lavrent'yev and N. M. Borovikova. *Gig Sanit* 36(1):55-59, 1971.

See also:

- * (Rev): 2168
- * (Chem): 2257
- * (Viral): 2348
- * (Immun): 2434

VIRAL CARCINOGENESIS

STUDIES ON THE RELATIONSHIP OF LEUKEMIA IN ANIMALS AND MAN. (E.) Maruyama, K. (U. as M.D. Anderson Hosp. Tumor Inst., Houston) and Omochowski. *Texas Rep Biol Med* 29(1):83-96, 1971.

Leukemias and sarcomas from animals and men were studied using immunological and ultrastructural techniques, and etiological and antigenic similarities were noted. Material included cultured cells of leukemia and/or sarcoma virus-infected BALB/c mice, cells of bone tumors of hamsters and rats, cells of feline, canine and equine lymphomas, and cells of human patients with various neoplasms. All tumors from animals with spontaneous or virus-induced tumors gave positive mixed hemadsorption reactions with immune sera against murine, feline Rauscher leukemia virus grown in human cells. Electron microscopy revealed C-type virus particles in cell cultures from all species examined, including cells from canine and equine lymphoma. C-type particles replicated in human cells infected with herpesvirus which had been derived from neoplastic cells by inoculation of feline or murine leukemia cells into a Burkitt's lymphoma culture. Herpesvirus particles disappeared in the human cells following replication of C-type virus particles in these cells. In cells from equine lymphoma and from patients with conditions such as thyroid carcinoma, a simultaneous infection of herpesvirus and C-type particles was seen.

DNA DENSITY OF ONCOGENIC AND NON-ONCOGENIC SIMIAN ADENOVIRUSES. (E.) Goodheart, C. (U. Microbiol., U. Illinois Med. Ctr., Chicago). *Virology* 44(3):645-648, 1971.

The density of the DNA from each of 16 simian adenoviruses was determined using CsCl density gradient centrifugation. The molar ratios of guanine and cytosine were also calculated. Densities were determined from the position of each of the viral DNA's on the density gradient relative to the position of bacterial markers *Clostridium perfringens*, *Escherichia coli* and *Micrococcus lysodeikticus*. The densities of these 3 markers were, resp., 1.691 g/ml, 1.710 g/ml, and 1.731 g/ml. The densities of the viral DNA's ranged from 1.709-1.721 g/ml, with a mean density of 1.7148 g/ml. The mean guanine-cytosine molar ratio for the viral DNA's was 55.76%. Considering the oncogenic and non-oncogenic viruses separately, the mean molar ratios of guanine and cytosine were 56.92% and 54.26%, resp. This difference was found to be statistically significant.

TRANSFORMATION OF MURINE CELLS BY TWO "SLOW VIRUSES," VISNA VIRUS AND PROGRESSIVE PNEUMONIA VIRUS. (E.) Takemoto, K. K. (Lab. Viral Dis., Natl. Inst. Allergy and Infect. Dis., Natl. Inst. Hlth., Bethesda, Md.) and L. B. Stone. *J Virol* 7(6):770-775, 1971.

Visna virus and progressive pneumonia virus (PPV) were prepared in sheep testis cell cultures and used to infect mouse cells in multiplicities of 10 plaque

forming U/cell. Three wk later, morphologically altered spindle-shaped cells began to appear in the cultures infected with the 2 viruses. Transformed cells were confined to separate foci within each culture, and there were 40-60 such foci per culture dish. Lines of transformed cells were established from the original infected cultures. On continued passage, the cells from the infected lines lost their initial fibroblastic appearance and became more epithelioid. Supernatants from transformed cultures did not transform other cells in culture. However, when transformed cells were cocultivated with sheep testis cells, the cells yielded virus by 3-4 wk after the beginning of cultivation; rescued virus was identified as visna or PPV. Neither RNA nor DNA tumor viruses, nor the antigens associated with these viruses, could be found in visna virus- or PPV-transformed cells. Transformed mouse cells produced small regressing tumors in untreated mice and large tumors in X-irradiated mice.

2298 TRANSFORMATION AND PRODUCTIVE INFECTION OF HUMAN OSTEOSARCOMA CELLS BY A FELINE SARCOMA VIRUS. (E.) McAllister, R. M. (U. Southern California Sch. Med. Los Angeles), J. E. Filbert, M. O. Nicholson, R. W. Rongey, M. B. Gardner, R. V. Gilden and R. J. Huebner. *Nature* 230(17):279-282, 1971.

A cell line (MT) derived from a human osteosarcoma was inoculated with feline sarcoma virus (FSV). By 19 days after infection, the FSV-infected cells showed a higher saturation density and a more rounded and tightly packed cell growth than the uninfected MT cultures. Infected MT cells released a virus which induced foci in embryo cells; these foci were similar to foci induced in beagle cell cultures by FSV. C-type particles were seen in FSV-infected MT cells after 3 passages *in vitro*; and infected cells reacted in complement-fixation tests with dog serum against feline C-type virus group specific and envelope antigens. While uninfected MT cells, inoculated into fetal cats, did not cause tumors, FSV-infected MT cells produced s.c. tumors in 2 of 4 cats given these cells. These tumors were fibrosarcomas similar to those induced in cats and dogs by FSV; and the tumors induced in the fetal cats by infected cells contained C-type virus particles.

2299 DNA AND THE RNA VIRUSES. (E.) Spiegelman, S. (Coll. Phys. Surgeons, Columbia U., New York City, N.Y.). *Proc Roy Soc Lond* 177(1046):87-108, 1971.

Incorporation of tritium-labeled thymidine triphosphate into acid-insoluble products were observed with serial transfer preparations of Rous sarcoma virus, Rauscher leukemia virus, feline leukemia virus, avian myeloblastosis virus, Moloney sarcoma virus, murine and monkey tumor viruses. Rous sarcoma virus and Rauscher leukemia virus DNA polymerases maintained linear synthesis for time periods extending to 8 hr, whereas the avian myeloblastosis virus, feline leukemia virus and

murine mammary tumor virus polymerases showed a tendency to slow down after about 90 min. Preparations which did not require pretreatment with detergent to exhibit activity were severely inhibited by the 0.2% detergent required to disrupt the virions. The acid-precipitable product was degraded by DNase but not by RNase, pronase or sodium hydroxide and had a density within the DNA range of 1.450. Results of an annealing reaction between ³H-labeled DNA synthesized with the Rauscher leukemia virus polymerase and a great excess of RNA purified from the virions showed that all the DNA synthesized by the polymerase had some complementarity to the viral RNA. Intermediates of the polymerase reaction isolated after 20 min were found to be DNA-RNA hybrids.

- 2300 DNA POLYMERASE ACTIVITY ASSOCIATED WITH PURIFIED KILHAM RAT VIRUS. (E.) Salzman, L. A. (Natl. Inst. All. Infect. Dis., Natl. Inst. Hlth., Bethesda, Md.). *Nature* 231(3):174-176, 1971.

DNA polymerase which was purified from Kilham rat virus in CsCl gradients showed maximal activity at pH 9 and was inhibited by EDTA, KCl and *p*-chloromercuribenzoate. All 4 deoxynucleotide triphosphates - dGTP, dCTP, dTTP and dATP - were required for maximal DNA polymerase activity. An external source of DNA was also required for maximal enzyme activity, and the enzyme activity increased with increases in enzyme protein. With salmon sperm DNA as a template, the enzyme reaction product was double stranded as judged from its buoyant density in CsCl equilibrium gradients and elution from hydroxyapatite column.

- 2301 VIRUSES AND RENAL CARCINOMA OF *RANA PIPIENS*: XI. ISOLATION OF FROG VIRUS 3 TEMPERATURE-SENSITIVE MUTANTS; COMPLEMENTATION AND GENETIC RECOMBINATION. (E.) Naegele, R. F. (St. Jude Children's Res. Hosp., Memphis, Tenn.) and A. Granoff. *Virology* 44(2):286-295, 1971.

Frog virus 3 was grown in fathead minnow cells and treated with 8×10^{-7} M 5-bromodeoxyuridine; 11 temperature-sensitive mutants were produced of which 6 were studied more fully. Taking the efficiency of plating of the parent frog virus as 1, it was found that the plating efficiency of the mutants at 30° ranged from 1.4×10^{-4} to 3.5×10^{-5} . The number of plaques formed by mutants at 25° ranged from 3.4×10^7 to 3.1×10^8 , while the number of plaques formed by mutants at 30° ranged from 1.2×10^3 to less than 1.0×10^4 . The yield of mutant viruses at 30° was 0.4-3.6% of the yield of mutants at 25°. It was shown that none of the mutants was more temperature-sensitive than wild-type frog virus 3. Five of the mutants studied were found to complement each other in mixed infection experiments; complementation levels ranged from 9-126. High recombination frequencies (e.g., 9-63%) were obtained with all mutants.

- 2302 ULTRASTRUCTURAL AND BIOLOGICAL PROPERTIES OF A CYTOMEGALOVIRUS RESCUED FROM A HUMAN PARANGLIOMA. (E.) Heine, U. (Natl. Cancer Inst. Natl. Inst. Hlth., Bethesda, Md.), J. Kondratieck, D. V. Ablashi, G. R. Armstrong and A. J. Dalton. *Cancer Res* 31(5):542-549, 1971.

When cells from a recurrent human paraganglioma placed in contact with WI-38 cells a virus appeared in the WI-38 cells which had the ultrastructural and antigenic properties of a cytomegalovirus. Original tumor tissue exhibited cells resembling lymphoblasts growing in suspension, and the cells sometimes were seen to contain cytoplasmic areas anastomosing tubular structures in contact with endoplasmic reticulum. The cytomegalovirus in the WI-38 cells produced no cytopathic effect in the cells; it was sensitive to ether treatment. The serum from the paraganglioma patient contained antibodies against cytomegalovirus but no antibodies against herpesvirus hominis or Epstein-Barr virus.

- 2303 CHICK EMBRYO LETHAL ORPHAN (CELO) VIRUS: SOME PHYSICAL AND IMMUNOLOGICAL PROPERTIES. (E.) Potter, C. W. (Dept. Med. Microbiology, U. Sheffield, Yorkshire, England), J. S. Oxford, J. C. Downie, M. M. Attwood and R. D. Hardy. *Virology* 44(2):418-424, 1971.

Chick embryo lethal orphan (CELO) virus was purified from virus-inoculated chicken eggs by equilibrium centrifugation in CsCl density gradients; the virus banded at 1.32 g/cm^3 , and this band was found to contain the peak infectivity virus titers. The thermal denaturation temperature of CELO DNA showed a base composition of 40% guanine-cytosine. CELO complement fixing antigens had the same sedimentation characteristics as did the complement fixing antigens of adenovirus 7. Under the electron microscope, the CELO virus was seen to contain icosahedral particles measuring 60-80 nm in diameter. When an immune serum against CELO was prepared in rabbits and reacted with CELO virus, it was found that the serum reacted with the virus antigens; the serum did not react, however, with adenovirus of various strains. No precipitin lines were formed between CELO antigen and sera prepared against adenovirus 12 antigen in immunodiffusion tests.

- 2304 INFLUENCE OF A LATENT VIRUS ON TRANSCRIPTION OF RNA-METHYLATING ENZYMES. (E.) Wainwright, E. (The New York Blood Ctr., New York). *Cancer Res* 31(5):710-715, 1971.

Cells of *Escherichia coli* K-12 W₆, irradiated with doses of UV light that induced phage development in 90-95% of the cells, were harvested at various intervals after irradiation, and the saturation level of tRNA-methylating capacity of extracts from such cells was measured. Total methylating capacity declined during incubation after irradiation, and a minimum level was reached at about 20 min postirradiation, followed by a rise in methylating activity to pre-

radiation levels. Total tRNA-methylating capacities of *E. coli* B and of several strains of *E. coli* 12 not carrying prophage were unaffected by similar irradiation; experiments with an isogenic pair of organisms with and without prophage also indicated that the transient drop in methylase activity was associated with prophage induction. Dialysates from extracts of UV-induced cells harvested between 10 and 30 min after irradiation inhibited tRNA methylation of extracts of logarithmically growing cells by about 50% indicating that the inhibitory action was the result of metabolic activity which followed UV treatment of prophage-carrying cells.

205 FOREIGN-CELL CONTAMINATION IN BURKITT TUMOURS. (E.) Fialkow, P. J. (Dept. of Pathology, U. Washington, Seattle), G. Klein, E. R. Blott, B. Gothoskar and P. Clifford. *Lancet* (1975):883-886, 1971.

Enzyme phenotypes of Burkitt's lymphomas were compared with those of tissue cultures derived from the lymphomas; the cell markers chosen were glucose-6-phosphatase and phosphoglucomutase. Twenty lymphoma tissue cultures established from 17 tumors from 13 patients with Burkitt's lymphoma were examined. In 6 of the 20 cultures it appeared that the cells were genetically foreign to the host from which they derived; foreign cells may have been present as minor populations in Burkitt's tumors at the time of biopsy. Blood transfusion and laboratory contamination were suggested as sources of the discordant cells.

206 AN INHIBITOR OF HERPESVIRUS HOMINIS IN EXTRACTS OF CULTURES OF BURKITT'S LYMPHOMA. (E.) Rabson, A. S. (Lab. Path., Nat. Cancer Inst., Nat. Inst. Hlth., Bethesda, Md.), S. A. Bressan and F. Y. Legallais. *Proc Soc Exp Biol Med* (1971):264-267, 1971.

Plaque formation in cultures of herpesvirus hominis (HSV)-infected human embryo kidney cells or rat kidney cells was inhibited 3-100-fold when treated with extracts from a jaw tumor of a Nigerian patient with Burkitt's lymphoma. Extracts from the Burkitt's lymphoma did not inhibit plaque formation in vesicular stomatitis virus-infected rat kidney cell cultures to the extent that these extracts inhibited plaque formation by HSV. Burkitt's lymphoma extracts also inhibited viral growth in HSV-infected cultures; titers of HSV in untreated cultures were 10-100-fold higher than in extract-treated cultures. Vesicular stomatitis virus growth was only slightly inhibited in extract-treated cultures. The HSV inhibitor in the Burkitt's lymphoma extract, which was sensitive to trypsin inactivation, did not appear to be interferon or an interferon inducer.

207 CHROMOSOME LESIONS INDUCED IN A HUMAN HEMATOPOIETIC CELL LINE BY INFECTION WITH EPSTEIN-BARR VIRUS. (E.) Huang, C. C. (Springville Labs., Roswell Park Mem. Inst., Springville, N.Y.), J. Minowada and J. S. Horoszewicz. *Proc Soc Exp Biol Med* 137(1):183-190, 1971.

Cell cultures prepared from the peripheral blood of a patient with myelogenous leukemia were inoculated with Epstein-Barr virus (EBV) isolated from a line of Burkitt's lymphoma cells. In uninfected hematopoietic cells from the leukemia patient, the modal chromosome number was 47, the incidence of polyploidy was 2% and a secondary constriction in the center of a D chromosome was seen in 61% of chromosomes studied. Cell viability declined in all cultures following EBV infection, but cultures infected with inactivated virus and uninfected cultures showed no impairment of growth; 96-108 hr postinfection, the number of cells/ml of culture in heat-inactivated EBV-infected cultures, uninfected cultures, and live EBV-infected cultures were 2×10^6 , 1.6×10^6 , and 4×10^5 , resp. EBV-infected cultures retained a modal chromosome number of 47. Chromosome aberrations induced by EBV infection included breaks which were most common in the subterminal and terminal regions. Many chromosomes had minute chromosome material attached to the end of an arm. No dicentric or exchange configurations were seen. Metaphases with pulverized chromosomes were another frequently seen aberration.

2308 MITOCHONDRIAL DNA FROM CELLS TRANSFORMED BY AVIAN MYELOBLASTOSIS VIRUS. (E.)

Riou, G. (Inst. Gustave Roussy, Villejuif, France) and F. Lacour. *Biochimie* 53(1):47-49, 1971.

Three-day-old chickens were inoculated with avian myeloblastosis virus (AMB); 2-3 wk later when the birds were in the terminal stages of leukemia, blood was collected and the mitochondrial DNA of transformed leukemic cells was examined and compared with that of normal cells. Liver and bone marrow cells from leukemic and normal birds were also compared. Examination by electron microscopy revealed that mitochondrial DNA from virus-transformed cells contained 74.4% monomers of circular DNA molecules which were sometimes twisted and sometimes open. Monomers comprised 95-96% of the mitochondrial DNA of normal cells. Virus-transformed cells contained mitochondrial DNA composed of 21.9% dimers and 3.7% catenated oligomers (e.g., trimers, tetramers and pentamers); normal cells had mitochondrial DNA composed of 4-5% dimers and no catenated oligomers.

2309 ALTERED TRANSFER RNA METHYLASE PATTERNS IN MAREK'S DISEASE TUMORS. (E.) Mandel, L.

R. (Merck Inst. Therapeutic Res., Rahway, N. J.), B. Hacker and T. A. Maag. *Cancer Res* 31(5):613-616, 1971.

A correlation was found between tumor development and infection with Marek's disease virus on the one hand and tRNA methylase activity in the liver and kidney of infected chicks on the other. The *in vitro* tRNA methylase activity in liver and kidney

homogenates from Marek's disease virus-infected birds was elevated 3-fold when compared to tRNA methylase activity in noninfected control birds. The tRNA methylase activity was increased in birds which had developed tumors, and was maximal in tumor nodules which were separated from adjacent tissue. Lung, heart and spleen tissue, which were nodule-free, did not show elevated tRNA methylase. Both normal and neoplastic liver were able to methylate heterologous methyl-deficient tRNA from *Escherichia coli*; however, only tumor-bearing liver tissue was able to methylate N⁷-methylguanosine, 3-methylcytidine, and 5-methyluridine.

- 2310 SIZE AND COMPOSITION OF MAREK'S DISEASE VIRUS DEOXYRIBONUCLEIC ACID. (E.) Lee, L. F. (Dept. Microbiology, U. Chicago, Ill.), E. D. Kieff, S. L. Bachenheimer, B. Roizman, P. G. Spear, B. R. Burmester and K. Nazerian. *J Virol* 7(3):289-294, 1971.

DNA was isolated from nucleocapsids of Marek's disease herpesvirus and cosedimented with T4 and with herpes simplex virus DNA in neutral sucrose or alkaline sucrose density gradients. The Marek's disease virus DNA was found to have a sedimentation constant of 56S, which corresponded to a molecular weight of 1.2×10^8 daltons. The most prominent band seen in the alkaline sucrose density gradients contained DNA sedimenting at 70S (molecular weight of 6×10^7 daltons). In hybridization experiments, the Marek's disease virus DNA hybridized with DNA of virus-infected cells but failed to hybridize with RNA of uninfected cells. On isopycnic sedimentation of the Marek's disease virus DNA with SPOL, *M. lysodeikticus* or herpes simplex virus DNA, the virus showed a density of 1.705 g/cm³.

- 2311 VIRAL INTERFERENCE IN FELINE LEUKEMIA-SARCOMA COMPLEX. (E.) Sarma, P. S. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.) and T. Log. *Virology* 44(2):352-358, 1971.

Feline embryo fibroblast (FEF) cultures infected with feline leukemia virus (FeLV) did not show overt signs of morphological transformation; infected cultures contained the FeLV group specific antigen and contained infectious virus. Superinfection of FeLV-infected cultures with related FeLV pseudotypes of murine sarcoma virus and feline sarcoma virus failed to transform the cultures, which appeared to be resistant to superinfection with these viruses; uninfected FEF cultures were susceptible to infection with the pseudotypes. This interference with the FeLV pseudotypes seemed to be specific for FeLV. When pseudotype FeLV of murine sarcoma virus was derived from the same strain of FeLV as that used for the initial infection, viral interference was always observed; however, when the challenge FeLV pseudotype used for superinfection was derived from a strain of FeLV other than the strain used for the initial infection, interference was not always seen.

- 2312 ISOLATION AND CHARACTERIZATION OF TWO GROUP-SPECIFIC ANTIGENS FROM FELINE LEUKEMIA VIRUS. (E.) Schäfer, W. (Max-Planck Tübingen, Germany), J. Lange, D. P. Bolognesi, de Noronha, J. E. Post and C. G. Rickard. *Virology* 44(1):73-82, 1971.

Purified feline leukemia virus was subjected to electrophoresis on polyacrylamide gels with the result that 3 major protein components were identified and designated EI, EII and EIII. EI was more electrophoretically mobile than EII, which was more mobile than EIII. The 3 proteins had molecular weights of 15,000, 18,000 and 33,000, resp. Rat murine leukemia virus had a similar electrophoretic mobility pattern to the feline leukemia virus, as avian leukemia virus had a different pattern. Antigens were isolated from feline leukemia virus which were electrophoretically similar to fractions EI and EIII. The EI isolate was regarded as a specific antigen found only in feline leukemia sarcoma viruses, whereas the EIII protein isolate was regarded as a group-specific antigen occurring in leukemia viruses of animal species other than cat.

- 2313 THE POTENTIAL FOR LEUKEMIA REGRESSION IN BALB/c MICE. (E.) Rich, M. A. (Dept. Biol., Res. Labs., Albert Einstein Med. Ctr., Philadelphia, Penna.) and M. Dietz. *Proc Soc Biol Med* 137(1):35-38, 1971.

ICR/Ha Swiss strain mice and BALB/c strain mice inoculated with conventional and regressing strains of Friend leukemia virus, and the onset and regression of symptoms of leukemia, including splenomegaly, were observed. Both mouse strains were susceptible to leukomogenesis by either strain of virus. Of the Swiss mice given conventional Friend virus, 1 and 8 of 10 given regressing virus developed leukemia with mean latencies of 14 days; all 9 of the BALB/c mice given conventional virus and 7 of 10 given regressing virus developed leukemia with latencies of 12 and 21 days, resp., for the 2 virus strains. 75% leukemia regression was seen among Swiss mice given regressing virus, but none of the BALB/c mice given regressing virus showed regression of leukemia. By 49 days postinfection, 2 of 18 Swiss mice and 1 of 16 BALB/c mice had died with leukemia. When the life span of leukemic BALB/c mice was prolonged by giving them reduced inocula of Friend virus, the mice still failed to show leukemia regression, suggesting that the failure of regression of leukemia in BALB/c mice was not due to the fact that death occurred before expression of regression could occur.

- 2314 TUMOR CELL MIGRATION. (E.) Cochran, A. J. (Karolinska Inst., Stockholm, Sweden). *Rev Europ Etud Biol* 16(1):44-47, 1971.

Cells from an ascitic mouse lymphoma originally induced by Moloney virus were placed in an open capillary tube (10^6 viable tumor cells/tube).

owed to migrate into a planchette containing growth medium. Incubation of the system at 37° increased the migration area; adding 5% CO₂ to the system also increased the area of migration. The area of migration of the tumor cells was decreased by incubation at low temperatures, by placing the tubes at an angle with open end up and by adding actinomycin D or actinomycin C to the system. Killing the tumor cells inhibited the migration of tumor cells altogether.

ANALYSIS OF THE FUSION OF XC CELLS INDUCED BY HOMOGENATES OF MURINE LEUKEMIA VIRUS-INFECTED CELLS AND BY PURIFIED MURINE LEUKEMIA VIRUS. (E.) Johnson, G. S. (Nat'l. Cancer Inst., Bethesda, Md.), R. M. Friedman and I. Pastan. *J Virol* 7(6):753-758, 1971.

Cultures of mouse embryo cells infected with murine leukemia virus were homogenized preparatory to being used as a fusion factor for tissue culture systems of the XC cell line, a Rous sarcoma virus-induced rat tumor. Syncytium formation occurred as a result of the fusion process; an increase in size and number of the multinucleated cells which reached completion within 48 hr was observed. Three general groups were recognized: 1) small multinucleated cells composed of 2-10 nuclei; 2) larger cells composed of about 10-30 nuclei, often accompanied by vacuoles and occasional nuclear fusion; and 3) extremely large cells composed of an indeterminate number of nuclei with extensive nuclear fusion and marked vacuolization. Size and number of cells was dependent upon the amount of fusion factor added. Fusion factor activity was detected in all of the particulate fractions of infected cell homogenates derived from centrifugation up to 35,000 xg but not in the 100 xg supernatant; greatest activity was seen in the 11,000 and 35,000 xg fractions. Trypsin at concentrations as low as 5 µg/ml completely destroyed fusion-stimulating activity whereas ribonuclease, deoxyribonuclease and neuraminidase had no effect.

MURINE LYMPHOMA INDUCED BY REOVIRUS 3. (E.) Phillips, P. A. (Dept. Microbiol., U. Western Australia, Perth), D. Keast, M. Walters and N. F. Stanley. *Pathology* 1:133-138, 1971.

5 mice of the Prince Henry strain inoculated intranasally with 10 LD₅₀ U of reovirus strain HEV, 10 survived the stage of acute virus infection. In 1 of these mice, a large thymic lymphoma with lung infiltration was found. The lymphoma consisted of uniform sheets of lymphocytic cells which completely destroyed the normal architecture of the thymic cells. Reovirus 3 was isolated from circulating leukocytes of the tumor-bearing mouse. Serum from this animal did not contain detectable antibodies to reovirus; reovirus antigen was found in spleen and in the thymic lymphoma. The reovirus-associated thymic lymphoma was transplantable into newborn mice, in which it

grew as a large tumor mass in the mesenteric lymph nodes.

2317 SERINE HYDROXYMETHYL TRANSFERASE ACTIVITY IN EXPERIMENTAL LEUKEMOSIS. (Rus.)

Sergeyev, A. V. (Inst. Exper. and Clin. Oncol. Acad. Med. Sci., U.S.S.R., Moscow), Yu. V. Bukin and M. O. Raushenbakh. *Probl Gemat* 16(3):41-45, 1971.

Spleen tissue of BALB/c mice with Friend virus-induced leukemia had an average 2.25 fold increase in specific serine hydroxymethyltransferase activity compared to controls. The activity of this enzyme in the liver tissue of mice with leukemia was approximately 2 times lower than in the hepatic cells of healthy mice. The *in vitro* sensitivity of serum hydroxymethyltransferase activity to a number of pyridoxal phosphate inhibitors (including hydrazine, hydroxylamine, semicarbazide, thiosemicarbazide, isonicotinylhydrazide and D-cycloserine) in the liver, spleen and ascites cells of mice with experimentally induced leukemia was practically the same for all 3 types of cells and was similar to the sensitivity of this enzyme in the hepatic tissue of healthy mice tested against the same compounds. D-cycloserine (600 mg/kg) administered i.p. twice to mice with experimentally induced Freund's leukemia produced an 87% inhibition of serum hydroxymethyltransferase activity in the splenic tissue and a 98% inhibition of this enzyme in the ascites cells of C57BL mice with Graffi's leukosis.

2318 ELECTRON MICROSCOPIC STUDIES OF TUMOR VIRUSES: I. ENTRY OF MURINE LEUKEMIA VIRUS INTO MOUSE EMBRYO FIBROBLASTS. (E.) Miyamoto, K. (Flow Lab., Inc., Rockville, Md.) and R. V. Gilden. *J Virol* 7(3):395-406, 1971.

Cultures of NIH Swiss mouse embryo cells were treated with 25 µg of DEAE-dextran and subsequently inoculated with Rauscher murine leukemia virus; the entry of the virus into the cells was observed under the electron microscope. As viruses came in contact with the cell membrane the viral envelope was seen to dissolve while the membrane itself remained intact; in other preparations, both the envelope and the membrane dissolved simultaneously as the virus came in contact with the cell, and the viral nucleoids passed into the cell cytoplasm. In some cases, the cell membrane dissolved and the viral envelope remained intact; in these cases, the intact virus particle entered the cell cytoplasm. In the cytoplasm the viral envelope became disrupted permitting release of viral nucleoids into cytoplasm. Viral envelopes were never seen to fuse with cell membranes. The interactions of virus with cell membranes were seen in immature C type virus particles as well as in mature particles.

2319 THE ACTIVATION OF LATENT LEUKEMIC VIRUSES. (Rus.) Mazurenko, N. P. (Inst. Exp. Clin. Oncol. Acad. Med. Sci., U.S.S.R., Moscow), V. I.

Ponomar'kov, Ye. I. Zharova, G. K. Gogichadze, Ye. S. Revazova and N. Ye. Osipov. *Vestn Akad Med Nauk SSSR* 26(3):18-23, 1971.

Splenic and lymphatic tissue from four dogs with reticulosis, reticulo-hemocytoblastosis, hemocytoblastosis and myeloleukosis and from CC57Br mice infected with Mazurenko's hemocytoblastosis reticulosis virus was homogenized, and the suspensions injected i.p. in doses of 2-3 ml/wk into newborn dogs and 0.05-1 ml/wk to newborn mice. Fifteen newborn dogs inoculated with the canine leukosis suspension and six puppies inoculated with mouse leukotic suspensions failed to develop leukemias, despite a 3-yr follow up. In 1 of 8 experimental groups of CC57Br mice inoculated with leukotic suspensions from dogs, 4 of 14 mice (28%) developed leukemia; the incidence of spontaneous leukemias in this strain did not exceed 0.5%. A leukemic virus isolated from the infected mice was identified as Mazurenko's hemocytoblastosis reticulosis virus. Reference is made to a 10-yr experimental period (1957-1967), during which CC57Br mice were found to be latent carriers of the hemocytoblastosis-reticulosis virus which was first activated by the smallpox vaccine virus and subsequently by material from leukemic dogs; the activation mechanism is not known.

2320 SEPARATION OF MURINE CELLULAR AND MURINE LEUKAEMIA VIRUS DNA POLYMERASES. (E.)

Ross, J. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), E. M. Scolnick, G. J. Todaro and S. A. Aaronson. *Nature* 231(23):163-167, 1971.

Crude extracts of uninfected and murine leukemia virus-transformed BALB/3T3 cells were tested for DNA polymerase activity with synthetic RNA-DNA or RNA-RNA hybrids as templates. In the normal cell line there were 2 peaks of DNA polymerase activity; peak I had poor activity when poly rA,dT (>100) was used as a template, while peak II responded well. Two peaks of DNA-dependent DNA polymerase activity were eluted from extracts of the transformed cell at the same effluent volumes as those from the normal, uninfected cells, with DNA polymerase peak I eluting slightly ahead of DNA polymerase peak II. Overall yields of activity from uninfected and transformed cells were comparable.

2321 BLOOD ASPARTYL TRANSCARBAMYLASE ACTIVITY IN RAUSCHER VIRUS INDUCED MURINE LEUKEMIA.

(E.) Cory, J. G. (Dept. Chem., U. South Florida, Tampa). *Haematologia* 4(3/4):303-310, 1970.

Mice were infected with Rauscher murine leukemia virus, and aspartyl transcarbamylase (ATC) activity was investigated in their blood; ATC in virus-infected mouse blood was increased 4-fold over ATC in blood of uninfected mice. The Michaelis constants for ATC activity in the blood of normal and virus-infected mice were 1.8×10^{-3} and 1.4×10^{-3} M, resp.; pH activity profiles for ATC in normal and virus-infected mice were also similar. ATC activity in infected mice was inhibited less by succinate and

maleate than ATC in normal mice; the inhibitor constants for succinate was 4-fold larger for blood ATC in infected mice than for blood ATC in uninfected mice. Blood ATC activity in infected mice was markedly more sensitive to the sulfhydryl inhibitors *p*-hydroxymercuribenzoate and *N*-ethylmaleimide than was blood ATC in uninfected mice.

2322 THE ERYTHROCYTE AS VIRUS CARRIER IN FRIEND AND RAUSCHER VIRUS LEUKEMIAS. (E.)

Rauscher, C. A. (Dept. Microbiol., U. Arizona, Tucson) and Schloss. *Cancer Res* 31(6):841-846, 1971.

The response of BALB/c mice inoculated with plasma from various erythrocyte fractions from Friend virus-Rauscher virus-infected animals was measured in terms of mean day of death and degree of infectivity. Blood fractions used were plasma, whole erythrocytes, sonically extracted erythrocytes, sonically extracted erythrocyte stroma, water-lysed erythrocytes, water-lysed erythrocyte stroma and wash medium. The percent infectivity of Friend virus-infected mice in blood fractions ranged from 83-100% and the mean day of death from 43.5-70.3; the sonically extracted water-lysed erythrocyte stroma fractions were the most competent. With Rauscher virus, the degree of infectivity was 23% for the wash medium and 100% for the other fractions; the mean day of death varied from 43.2-75.8. The infected erythrocytes from Friend virus-infected mice showed increased osmotic fragility but not the erythrocytes from Rauscher virus-infected mice. Association of the virus with the erythrocyte could be due to physical adsorption of the virus to the infected plasma or due to infection and transmembrane production of an erythrocyte precursor and subsequent production of virus during maturation to erythrocyte.

2323 COMPLETE FREUND'S ADJUVANT STIMULATION OF RAUSCHER VIRUS-INDUCED LEUKEMOGENESIS.

(Rus.) Ter-Grigorov, V. S. (P. A. Herzen Res. Inst. Oncol. Acad. Med. Sci., U.S.S.R., Moscow), I. S. Irlin, O. Ya. Moskovkina and V. M. Bergol'ts. *Vopr Onkol* 17(2):54-59, 1971.

Freund's complete adjuvant (CFA) administered i.p. (0.1 ml) either 1 wk before or simultaneously with an i.p. injection of Rauscher virus-containing plasma (0.2 ml per animal) stimulated leukemogenesis in a sensitive line of BALB/c mice. Post-mortem examinations indicated increased splenomegaly, increased amounts of leukemic plaques below the splenic capsule, increased viral multiplication and generally earlier mortality of the mice compared with controls infected solely with the Rauscher virus. When administered to mice genetically resistant to the leukemogenic effects of the Rauscher virus, CFA in association with the virus inhibited this resistance and produced two distinct varieties of the pathology in the C57BL/6 strain; in one group inhibition of the leukemogenic resistance was transient and the Rauscher disease regressed, while in other cases irreversible progression of leukemia, sometimes with lympholeukosis, occurred. Four possible hypotheses for CFA stimulation of leukomogenesis are

discussed: a rapid increase in the number of mouse cells sensitive to the leukemogenic viral transformation; stimulation and disruption of the humoral immune response; suppression of the immunological cellular type reaction; inhibition of interferon production.

24 INFECTION OF SIMIAN ADENOVIRUS SA7 IN HAMSTER KIDNEY AND EMBRYO CELLS. (E.) Iino, T. (Res. Inst. Microbial Diseases, Osaka U., Japan) and M. Takahashi. *Biken J* 13(4):303-312, 1970.

Primary hamster kidney (Ham K) and embryo (Ham E) cells, primary African green monkey kidney (AGMK) cells and human embryo kidney and lung cells were inoculated with simian adenovirus SA7 in input multiplicities of 10-50 PFU/cell. In AGMK cells, an increase in infectious virus was seen 24 hr postinfection; at 20 hr postinfection, the virus yield from AGMK cells was $4.5 \log_{10}$ TCID₅₀/ml, while at 48 hr postinfection, the yield was more than $8 \log_{10}$ TCID₅₀/ml. Cytopathic changes were seen in AGMK cells by 13 hr postinfection, and basophilic inclusions were seen in most cells by 24 hr postinfection. Tumor and virus antigens were seen in nearly all AGMK cell nuclei by 24 hr. No significant replication of infectious virus was seen in Ham K or in Ham E cells infected with SA7. Morphological changes induced in Ham K cells by virus included eosinophilic inclusions surrounded by a halo in the nuclei and nuclear degeneration including eosinophilic and basophilic inclusions. Some Ham K cells remained intact through virus infection, and subsequently replicated to give rise to transformed cells. Tumor and viral antigens were seen in the nuclei of 50-60% of Ham K cells and in the nuclei of 20-30% of Ham E cells by 48 hr postinfection. In both Ham K cells and Ham E cells, increased DNA synthesis was seen at an early stage of virus infection; increased viral DNA synthesis was seen at an early stage of virus infection; increased viral DNA synthesis was also observed. Virus replication was seen in infected human cells, but the virus yields were about 1 hundredth of that seen in AGMK cells. Eosinophilic inclusions and basophilic inclusions were seen in human cells by 24 hr postinfection, and tumor and virus antigen were seen in the nuclei by 24 hr postinfection; nuclear degeneration occurred by 58 hr postinfection.

25 THREE SIZE-CLASSES OF INTRACELLULAR ADENOVIRUS DEOXYRIBONUCLEIC ACID. (E.) Worthingham, B. T. (Dept. Cell Biol., Sch. Med. U. Maryland, Baltimore) and W. Doerfler. *J Virol* 7(6):7-719, 1971.

Productive or nonproductive infection of KB cells by human adenovirus 12 (Ad 12) strain Huie or Ad 2 strain Benoit 6 resulted in the synthesis of 3 classes of viral DNA: a class which sedimented in alkaline sucrose gradients > 45S; a species which sedimented with DNA extracted from infectious adenovirions; and a class which sedimented at 18S. Purified adenovir-

ions with ³H-labeled DNA as inoculum permitted the fate of the parental adenovirus DNA to be followed; more than 90% of the label incorporated into the cells was acid precipitable. The fast-sedimenting class of adenovirus DNA that varied between 45-80S (probably due to mechanical breakage of cellular DNA) specifically hybridized with the viral RNA. The hybridization to cellular DNA was variable and ranged from 0.1-5%. Control experiments with recovery of added ¹⁴C-Ad DNA indicated that the fast-sedimenting label from infected cells was comprised of viral genetic material; the complete sensitivity of this material to deoxyribonuclease treatment suggested that this class DNA is uncoated within the cell. An adenovirus DNA which cosedimented with Ad 12 marker DNA also sedimented at 33S in alkaline sucrose gradients and at 29S (34S and 32S for Ad2-DNA) in neutral sucrose gradients; this DNA underwent hybridization only to viral DNA and not to cellular DNA. Essentially all of this class of adenovirus DNA was susceptible to deoxyribonuclease, which indicated that it too was uncoated. The slow-sedimenting DNA also hybridized only to viral DNA and was sensitive to deoxyribonuclease. Correlation of the amounts of label in each DNA class with time indicated that the parental Ad 2 or Ad 12 DNA is cleaved into 18S fragments which may become linked to the fast-sedimenting cellular DNA and serve as precursors to the integrated form of Ad DNA. Inhibition of macromolecular synthesis with thymidine, actinomycin D or cycloheximide had little effect on the formation of the slowly sedimenting species of viral DNA. These results suggest that the 18S viral DNA is not synthesized but is formed by an endonuclease within the cell or the adenovirion.

2326 THE HISTOPATHOLOGY OF TUMORS INDUCED BY PARA-ADENOVIRUS 7 TRANSFORMED CELL CLONES. (E.) Pauluzzi, S. (Inst. Infect. Dis., Perugia U., Italy), R. Ribacchi, R. Frongillo and M. P. Zeppa. *Europ J Cancer* 6(6):537-543, 1970.

Factors contributing to the morphological and antigenic heterogeneity of PARA-adenovirus hybrid-induced tumors were investigated. Two para-cell clones, 819/R/A2a and 928/R/B/Str were isolated from the first *in vitro* passages of PARA-adenovirus 7-induced hamster tumor cells. Both clones induced transplanted tumors similar to primary or transplanted tumors induced by adenovirus 7, adenovirus 12 or simian adenovirus 7 and quite different from SV40-induced tumors. Histological examination revealed undifferentiated small-cell tumors with hemorrhagic necrosis and typical multinucleate giant cells. However, the cell clone 928/R/B/Str revealed both adenovirus T and SV40 T antigens in almost 100% of the cells, while 819/R/A2a cells showed only SV40 T antigen upon immunofluorescence testing. These antigenic characteristics were maintained even after several passages *in vitro*. The uniform morphology of the tumors induced by the 2 investigated PARA-cell clones and the antigenic constancy of these clones indicated that PARA-transformed cells could not differentiate into various morphologic and antigenic phenotypes. Apparently the coexistence of cells which differ morphologically and antigenically in the same PARA-tumor starts from the very beginning of the oncogenic process.

- 2327 ISOLATION OF TEMPERATURE-SENSITIVE MUTANTS OF ADENOVIRUS TYPE 5. (E.) Williams, J. F. (Inst. Virol., Glasgow, Scotland), M. Gharpure, S. Ustacelebi and S. McDonald. *J Gen Virol* 11(2): 95-101, 1971.

Cultures of adenovirus type 5 were treated with either nitrous acid (0.7 M), hydroxylamine (1 M), or 5-bromodeoxyuridine (15 or 30 µg/ml virus culture on HeLa cells). These treatments produced a temperature-sensitive viral mutant strain which showed 1000-fold higher plaque-forming efficiency at 31° than at 38°. The frequency of these mutants in the surviving fractions of virus treated with nitrous acid and hydroxylamine was 8.4 and 9.6%, resp., while the frequency of the mutants in surviving fractions of virus treated with 5-bromodeoxyuridine was 0.55%. Most temperature-sensitive mutants were stable and showed little evidence of leakiness or back mutation.

- 2328 A CYTOCHEMICAL STUDY OF BASIC PROTEINS IN ADENOVIRUS-INFECTED CELLS. (E.) Russell, W. C. (Natl. Inst. Med. Res., London, England), E. Broadaty and J. A. Armstrong. *J Gen Virol* 11(2): 87-93, 1971.

Human embryonic kidney cells were infected at input multiplicities of 200 PFU/cell with adenovirus type 5 and infected cells were stained with phenanthrenequinone and with copper phthalocyanin-neutral red for detection of the presence of arginine in the infected cells. Stained preparations showed ring-like and rosette structures under the microscope; the structures were also seen on staining with fluorescent adenovirus P antiserum. Pretreatment with benzil blocked the cytochemical staining of the adenovirus-infected cells. The rings and rosettes were thought to be sites of arginine accumulation.

- 2329 THE RESPONSE OF BHK21 CELLS TO INFECTION WITH TYPE 12 ADENOVIRUS. V. STIMULATION OF CELLULAR RNA SYNTHESIS AND EVIDENCE FOR TRANSCRIPTION OF THE VIRAL GENOME. (E.) Raska, K., Jr. (Rutgers Med. Sch., Rutgers U., New Brunswick, N.J.), W. A. Strohl, J. A. Holowczak and J. Zimmerman. *Virology* 44(2):296-306

Cultures of baby hamster kidney cells BHK21/13 were infected with adenovirus type 12, and the incorporation of ³H-uridine into cellular RNA was compared in infected and in uninfected cells. BHK21 cells were abortively infected in the G₁ phase of the mitotic cycle. Infected cells showed a 3-5-fold increase in label uptake compared to uninfected cells. Incorporation of label into DNA was 10-15-fold higher in infected cells than in uninfected cells. Uridine kinase activity was found to be increased in the infected cells; the 45S, 32-28S, 18S and 4S species of cellular RNA were all synthesized at an increased rate in infected cells. By 12-14 hr after infection, it could be seen that infected cells were synthesizing virus-specific RNA; this RNA sedimented in the 18S

area of the sucrose gradient, and was thought to be the virus messenger in the cells.

- 2330 THE ULTRASTRUCTURE AND NATURE OF ADENOVIRUS TYPE 2-INDUCED PARACRYSTALLINE FORMATIONS. (E.) Henry, C. J. (William H. Singer Memorial Inst. Allegheny General Hosp., Pittsburgh, Pa.), M. Slifkin, L. P. Merkow and M. Pardo. *Virology* 44(1):215-218, 1971.

Vero or HeLa cell cultures were infected with adenovirus type 2 for 48 or 70 hr and sections of infected cultures were examined under the electron microscope. Infected cells showed crystalline arrays of virus particles, paracrystalline structures and 3 general types of intranuclear inclusion bodies. In some Vero cells, mature virus particles were seen in close association with the periphery of the cytoplasmic crystals. These crystals varied in size and shape. Crystals developed in both the cytoplasm and nucleus of virus-infected Vero cells, whereas crystals were found only in the nucleus of infected HeLa cells. Crystals were eosinophilic but devoid of nucleic acids. Paracrystals were composed of viral capsid antigens.

- 2331 CHROMOSOME TRANSPLANTATION AND TUMOUR ANTIGEN STUDIES OF THREE VIRUS-INDUCED TUMOUR CELL LINES. (E.) Potter, A. M. (Lodge Moor Hosp. Sheffield, England), C. W. Potter and J. S. Oxford. *Arch Ges Virusforsch* 33(1/2):61-71, 1971.

Cell lines derived from hamster tumors induced by adenovirus 12 (Tad III and H212) and by SV40 were inoculated s.c. into hamsters; the cell lines had been passaged more than 200 times *in vitro* and all cells contained specific virus-induced tumor antigens. The SV40-induced tumor cells and the Tad III tumor cells produced tumors in recipient hamsters, while the H212 cell line did not produce tumors in adult hamsters but did produce tumors in newborns. Tad III cells contained relatively low complement fixing titers for tumor antigens while H212 cells contained high complement fixing titers. Marker chromosomes were found to be most common in SV40-induced tumor cells and lowest in H212 tumor cells. Polyploidy was more common in virus-induced tumor cells than in normal hamster cells.

- 2332 STUDIES OF NONDEFECTIVE ADENOVIRUS 2-SIMIAN VIRUS 40 HYBRID VIRUSES: III. BASE COMPOSITION, MOLECULAR WEIGHT, AND CONFORMATION OF THE AD2+ND₁ GENOME. (E.) Crumpacker, C. S. (Natl. Inst. Allergy and Infectious Diseases, Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), E. Henry, T. Kakefuda, W. P. Rowe, M. J. Levin and A. Lewis, Jr. *J Virol* 7(3):352-358, 1971.

The nondefective hybrid of SV40 and adenovirus 2, designated Ad2+ND₁, was found to contain DNA with a buoyant density of 1.715 g/cm³ and a thermal denaturation profile of 75.1 C; both these values were

closely similar to those calculated for the DNA of nonhybrid adenovirus 2. The molecular weight of 12^+ND_1 DNA was found to be about 22×10^6 to 25×10^6 daltons and that of adenovirus 2 itself was 13×10^6 to 25×10^6 . All the DNA molecules in 12^+ND_1 virus were double-stranded and linear. It was estimated that the hybrid virus contained about one-tenth of the SV40 genome, or 220×10^3 to 250×10^3 daltons of SV40 DNA.

333 SOME INDICATORS OF CARBOHYDRATE METABOLISM IN TISSUE CULTURE, IN PRIMARY CONTACT WITH ONCOGENIC VIRUSES AND IN SARCOMAS INDUCED BY ADENOVIRUS-12. (E.) Ageenko, A. I. (Hertzen Res. Inst. Oncol., Moscow, U.S.S.R.) and N. Kholmukhamedova. *Biia Biol (Praha)* 17(1):13-17, 1971.

The dynamics of carbohydrate metabolism following primary contact with oncogenic or infectious virus were investigated in Wistar rat embryo cell monolayer cultures. Human adenovirus type-12, -3 or -6 grown in cell culture was used in a dose of 10^3 - 10^4 TCID₅₀/0.1 ml (tissue culture infectious dose). Aerobic and anaerobic glycolysis rates appeared to be highest in the adenovirus-type-12-infected cell cultures reaching maximal values at 40 hr after inoculation. Enhanced oxygen consumption was maximal 4 hr following inoculation with all 3 types of adenovirus returning to normal values at 120 hr after the beginning of the experiment. Aldolase and lactate dehydrogenase activities were highest in the adenovirus type-12-infected cultures with maximal plateau values between 48-72 hr and 96-168 hr following inoculation. The infectious titer of adenovirus type-3 and adenovirus type-6 increased during the 1st hr and reached maximal values 72 hr following inoculation; no such increase was observed with adenovirus type 12.

334 PERSISTENT INFECTION WITH HERPES SIMPLEX VIRUS *IN VITRO*. II. EFFECT OF ANTIBODY ON THE COURSE OF HERPETIC PERSISTENCY IN EARLE'S CELLS. (E.) Nii, S. (Res. Inst. Microbial Diseases, Osaka U., Japan). *Biken J* 13(4):339-352, 1970.

Cultures of Earle's L cells persistently infected with herpes simplex virus were grown in medium containing either human antiserum or human γ globulin; the spread of the cytopathic effect in infected cultures was reduced by the antibody treatment, and after 1 month in culture no cytopathic foci were to be seen in the infected cells. However, virus persisted in the cells in most cultures for 1-8 months. Subcultures of infected cells treated with antibody retained virus even when grown in antibody-containing medium in the course of subculturing. In cells subcultured without antibody, cytopathic changes appeared earliest in fresh cultures. In some infected cultures without antibody, infectious virus and cytopathic changes were not detected until a latent period had elapsed. Although virus spread in Earle's L cells in the presence of antibody was

arrested, virus spread in BSC1 cells infected with virus in the presence of antibody was not as markedly suppressed.

2335 GUINEA PIG LEUKOCYTES; *IN VIVO* AND *IN VITRO* INFECTION WITH A HERPES-LIKE VIRUS. (E.) Hsiung, G. D. (VA Hosp., West Haven, Conn.), C. K. Y. Fong and K. M. Lam. *J Immunol* 106(6):1686-1689, 1971.

Hartley strain guinea pigs were given inoculations of 10^6 TCID₅₀/ml of a Herpes-like virus (HLV) suspension, and the animals were killed thereafter and leukocyte cultures were prepared and examined by electron microscopy. In some cases guinea pig leukocytes were infected *in vitro* with HLV. Although HLV particles were seen in leukocytes established in 3-day cultures from infected animals, no virus particles were found in leukocytes taken directly from infected guinea pigs. When guinea pigs leukocyte cultures were infected *in vitro* with HLV, it was found that there were more viable leukocytes in the infected cultures than in the control uninfected cultures.

2336 TRANSFER OF THYMIDINE KINASE TO THYMIDINE KINASELESS L CELLS BY INFECTION WITH ULTRAVIOLET-IRRADIATED HERPES SIMPLEX VIRUS. (E.) Munyon, W. (Roswell Park Mem. Inst., Buffalo, New York), E. Kraiselburd, D. Davis and J. Mann. *J Virol* 7(6):813-820, 1971.

Herpes simplex virus (HSV) suspensions were exposed to UV for 1-18 min in amounts of 23 ergs/mm²/second; irradiated virus was used to infect cultures of L₁ cells which lacked thymidine kinase activity (Ltk⁻ cells). The transformation of Ltk⁻ to Ltk⁺ cells in virus-infected cultures was measured by the formation of colonies of Ltk⁺ cells in a supplemented growth medium. No colony formation was observed with uninfected L cells, or with cells infected with unirradiated HSV, but colony formation was seen with cultures infected with irradiated HSV; the maximum frequency of Ltk⁻ to Ltk⁺ transformation was about 10^{-3} . Cell lines of HSV-transformed Ltk⁺ cell lines contained 7-24 times as much thymidine kinase activity as did parental Ltk⁻ cells. Optimal formation of Ltk⁺-transformed cell colonies was seen in cultures infected with HSV which had been irradiated with UV for 9-12 min. The number of Ltk⁺-transformed colonies formed was proportional to the dose of virus. Substitution of bromodeoxyuridine for thymidine in the supplemented growth medium, which was infected with irradiated HSV, suppressed colony formation. A mutant strain of HSV which failed to induce thymidine kinase activity during lytic infection failed to cause the Ltk⁻ to Ltk⁺ transformation. This transformation may have been caused by the transfer of a viral gene to the Ltk⁻ cells; alternatively, the transformation may have been caused by the promotion of expression of a repressed cellular enzyme by a product of the viral gene.

- 2337 DEOXYRIBONUCLEIC ACID SYNTHESIS IN SYNCHRONIZED MAMMALIAN KB CELLS INFECTED WITH HERPES SIMPLEX VIRUS. (E.) Cohen, G. H. (Center for Oral Hlth. Res., U. Pennsylvania, Philadelphia), R. K. Vaughan and W. C. Lawrence. *J Virol* 7(6): 783-791, 1971.

Mammalian KB cells were infected with herpes simplex virus (HSV) at various times after synchronization of cells by double thymidine block; an unscheduled round of viral DNA synthesis occurred 2-3 hr after infection of the synchronized cells, regardless of the time in the cell cycle that the infectious virus was introduced. In a related experiment, synchronized KB cells were infected with HSV at 3, 5, 8, and 11 hr after reversal of the thymidine block and the time-course of infectious virus formation was observed. In each case, increases in progeny virus were seen 6 hr postinfection, with maximum titers of virus occurring 11-12 hr postinfection. A similar cycle of viral replication was seen in all infected cultures without regard to the time of virus infection relative to the mitotic phase of the cells. When KB cells were infected with HSV at a time when host cell DNA synthesis was minimal (11 hr after the beginning of cell synchrony), viral DNA synthesis began 2-3 hr postinfection; viral DNA synthesis attained maximum levels by 4 hr postinfection and dropped off by 8 hr postinfection. HSV infection may have inhibited synthesis of KB cell DNA and the initiation of the S phase of mitosis.

- 2338 VIRUSES AND RENAL CARCINOMA OF *RANA PIPPIENS*: X. COMPARISON OF HERPES-TYPE VIRUSES ASSOCIATED WITH LUCKE TUMOR-BEARING FROGS. (E.) Gravell, M. (St. Jude Child. Res. Hosp., Memphis, Tenn.). *Virology* 43(3):730-733, 1971.

The base compositions of Rafferty isolate (frog virus 4, FV4) DNA and herpes-type virus (L-HTV) DNA from Lucke tumors were estimated from their melting profiles. The guanine plus cytosine (G + C) contents calculated from the T_m values for FV4 and L-HTV DNA were 54% and 45%, resp. The base composition of FV4 DNA estimated from its equilibrium buoyant density in $CsCl_2$ was 56% G + C; FV4 DNA banded at a density of 1.715 g/ml. DNA:DNA hybridization studies to detect homologous sequences with DNA from FV4, L-HTV, cultured adult frog kidney cells and a polyhedral cytoplasmic DNA virus showed that FV4 DNA hybridized with homologous DNA up to 70.6% but less than 1.56% with any heterologous DNA. Virus neutralization tests with FV4 and L-HTV antisera showed no cross-reactivity between the 2 viruses, further indicating that FV4 and L-HTV are different viruses.

- 2339 SYNERGISTIC EFFECT OF HERPES SIMPLEX VIRUS AND CYTOSINE ARABINOSIDE ON HUMAN CHROMOSOMES. (E.) O'Neill, F. J. (Milton S. Hershey Med. Ctr. Pennsylvania State U., Hersey, Pa.) and F. Rapp. *J Virol* 7(5):692-695, 1971.

Logarithmically growing human embryonic lung cells were inoculated with herpes simplex virus type 2

(5 PFU/cell) together with 10 μ g of cytosine arabinoside (ara-C). Of 225 cells examined after treatment with virus (strain 333) and ara-C, 9 cells had 1 chromosome break, 7 cells had 2 breaks and 78 cells had 3 or more breaks. In addition, 27 cells showed secondary constrictions. In human embryonic lung cells treated with herpes simplex virus alone, 15 cells had 1 chromosome break, 4 had 2 breaks and 1 had 3 or more breaks, while 33 cells had secondary constrictions. In cells treated with ara-C alone, 37 cells had 1 chromosome break, 13 had 2 breaks and 13 had 3 or more breaks, while 3 cells had secondary constrictions. Cells not treated with either virus or ara-C had 4 cells with 1 break, 1 cell with 2 breaks and no cells with 3 or more breaks, while 2 cells showed secondary constrictions. It was thought that herpes simplex virus and ara-C acted synergistically to promote chromosome changes in the human lung cells.

- 2340 IN VITRO INDUCTION OF A HERPES-TYPE VIRUS IN "SUMMER-PHASE" LUCKE TUMOR EXPLANTS. (E.) Breidenbach, G. P. (Dept. Microbiol., Tulane U., New Orleans, La.), M. S. Skinner, J. H. Wallace and M. Mizell. *J Virol* 7(5):679-682, 1971.

Tumor cells from a Lucké "summer phase" renal adenocarcinoma of *Rana pipiens* were incubated at 15.5°, 11.5° or 7.5°C for 8-14 wk. The Lucké "summer phase" tumor developed at 22°-26°C on frogs collected during the summer and on frogs maintained in the laboratory; a "winter phase" tumor form was found on frogs during the cooler months and on frogs maintained in the laboratory at or below 7.5°C. 14 of the 6 explants from the summer phase tumors kept at 7.5°C, 3-5% of the nuclei were seen to be enlarged by 14 wk in culture and 1% of the cells showed type A virus particles. Empty or complete herpes virus particles were seen in the nuclei of cells kept at 7.5°C.

- 2341 LYMPHOID CELL-CULTURE LINE DERIVED FROM LYMPH NODE OF MARMOSET INFECTED WITH HERPESVIRUS SAIMIRI--PRELIMINARY REPORT. (E.) Rabson, A. S. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth. Bethesda, Md.), G. T. O'Connor, D. E. Lorenz, R. L. Kirschstein, F. Y. Legallais and T. S. Tralka. *J Nat Cancer Inst* 46(5):1099-1103, 1971.

Marmoset monkeys infected with *Herpesvirus saimiri* developed malignant lymphoma, and a lymphoid cell line designated MLC-1 was derived from the lymph node of affected marmosets. Three months after initiation of the cell culture very few MLC-1 cells containing intranuclear herpesvirus particles were found, and virus could not be isolated from frozen and thawed MLC-1 cell pellets or culture supernatants. However, a herpesvirus could be isolated from cell cultures produced by co-cultivation of MLC-1 cells with Vero monkey kidney cells. This herpesvirus produced smaller plaques than *H. saimiri* and appeared to be antigenically related to that virus. In MLC-1 cultures of 5 mo. standing the *H. saimiri*-like virus could occasionally be isolated from cell supernatants. When inoculated into marmoset

sets, the *H. saimiri*-like virus produced a malignant condition similar to that produced by *H. saimiri*; however, the condition produced by the *H. saimiri*-like virus was characterized by more necrosis and less lymphoreticular cell proliferation than was seen in marmosets infected with *H. saimiri* itself.

- 2342 EARLY EVENTS REQUIRED FOR INDUCTION OF CHROMOSOME ABNORMALITIES IN HUMAN CELLS BY HERPES SIMPLEX VIRUS. (E.) O'Neill, F. J. (Milton S. Hershey Med. Ctr., Pennsylvania State U., Hershey) and F. Rapp. *Virology* 44(3):544-553, 1971.

When logarithmically growing cultures of human embryonic lung cells were infected overnight with 2 or 5 PFU of herpes simplex virus (HSV), the number of cells with chromosome aberrations was significantly increased in comparison to uninfected cells. Abnormalities observed in virus-infected cultures included chromosome breaks, secondary constrictions and erosion. When cells were pretreated with human interferon prior to virus infection, the incidence of chromosome abnormalities in infected cultures did not exceed that in uninfected cells, suggesting that chromosome abnormalities are induced by virus infection following the uncoating of the viruses, and that the induction of aberrations requires some translation of the viral genome. When cytosine arabinoside (10 µg/ml) or iododeoxyuridine (25 to 100 µg/ml) were added to cell cultures following virus infection, virus multiplication in the infected cells was inhibited by more than 99.9%; however, neither cytosine arabinoside nor iododeoxyuridine inhibited the induction of chromosome abnormalities by HSV. Apparently, viral induction of chromosome aberrations occurs at a period preceding viral DNA synthesis. Cytosine arabinoside appeared to potentiate the induction of aberrations by HSV.

- 2343 LYMPHOID CELL LINES: ACTIVATION OF A LATENT HERPES-LIKE VIRUS PARTICLE? (E.) McCormick, K. J. (Baylor Coll. Med., Houston, Tex.), D. M. Mumford, W. A. Stenback and J. J. Trentin. *Nature* 230(11):83-84, 1971.

Antigenic conversion of 2 lymphoid cell lines grown *in vitro* is described. One cell line was derived from a patient with Burkitt's lymphoma and cultured for 6 months (11 passages) before the presence of herpes virus particles or of complement fixing (CF) antigen could be ascertained. Another cell line derived from a child suspected of having infectious mononucleosis revealed the presence of herpes-like virus particles and indirect immunofluorescence (IF) antigen after 2.5 yr of cell culture. By that time the cells became positive by CF with African sera. These antigenic conversions seem to indicate that the genetic information for virus production is carried in apparently virus-negative cell lines.

- 2344 MOUSE MAMMARY TUMORIGENESIS BY MAMMARY TUMOR VIRUS IN THE ABSENCE OF THYMUS, SPLEEN OR BOTH ORGANS. (E.) Squartini, F. (Med. Sch., U. Pisa, Italy). *Israel J Med Sci* 7(1): 26-35, 1971.

Mice of various strains underwent thymectomy at 1 day-of-age or splenectomy at 2 days-of-age, or both operations; all the mice strains used except one carried a spontaneous infection with mammary tumor virus (MTV). In a group of female BALB/c (MTV-free) mice injected with MTV after undergoing thymectomy, 39% of animals developed hyperplastic alveolar mammary nodules, whereas the percentage of intact mice developing nodules in groups given MTV was 100%; the percentage of intact mice developing nodules in groups not given MTV was 20%. The incidence of pregnancy-dependent mammary tumors or plaques was observed in BALB/cf(RIII) MTV-infected mice; in intact mice, mammary tumors were pregnancy-dependent to some degree in 81.5% of the cases, whereas in thymectomized mice, tumors were partially pregnancy-dependent in only 23% of the cases. In intact BALB/cf(C3H) mice frank mammary tumors developed in 82% of cases, whereas thymectomized mice of the same strain developed lesions in 46% of cases. Thymectomy also prolonged the latent period for the appearance of these tumors. In force-bred mice the incidence of mammary tumor development was similar to that in intact mice. Thymectomy did not affect the frequency of mammary tumors in RIII strain mice. In splenectomized BALB/cf(C3H) mice, the incidence and latency of mammary tumor development was reduced; tumors developed in 82% of intact mice and in 52% of splenectomized mice. In mice of this strain which underwent both thymectomy and splenectomy, splenectomy partially suppressed the depressive effect of thymectomy on tumor development; splenectomized and thymectomized mice had tumor incidence patterns similar to those seen in intact mice. Splenectomy did not affect tumor incidence in RIII strain mice.

- 2345 POSSIBILITY OF A DNA-CONTAINING MAMMARY TUMOR VIRUS IN RED BLOOD CELLS OF MOUSE. (E.) Nandi, S. (Dept. Zool., U. California, Berkeley). *Nature* 230(13):146-147, 1971.

The RBC fraction was separated from the blood of 6-8 wk old BALB/cfC3H mice infected with mammary tumor virus and incubated with various proteases and nucleases for 2 hr at 37° either singly or in combination. Neither proteases nor nucleases were able to destroy the infectivity of the RBC fraction; however, the addition of RNase or DNase following treatment with protease caused complete inactivation. However, when DNase or RNase was previously treated with a nuclease inhibitor, the effect was lost. These results demonstrate the nucleoprotein nature of the infective moiety designated as R-MTV.

- 2346 INHIBITION OF SPONTANEOUS MAMMARY CARCINOMA OF MICE BY TREATMENT WITH INTERFERON AND POLY I:C. (E.) Came, P. E. (Dept. Microbiol., Schering

Corp., Bloomfield, N. J.) and D. H. Moore. *Proc Soc Exp Biol Med* 137(1):304-305, 1971.

Strain RIII mice were given 100 µg doses of polyinosinic acid:polycytidylic acid (poly I:C), 1000-2500 U interferon, normal mouse serum or no treatment (control), and the incidence of mammary tumor development and the appearance of mammary tumor virus in mammary milk were observed in the 4 treatment groups. Normal mouse serum did not reduce the incidence of spontaneous tumors from that seen in the control group; by 35 wk after treatment, nearly 100% of the control mice had tumors, and nearly 100% of mice given normal serum had tumors. Poly I:C and interferon both inhibited the rate of tumor development; by 35 wk after treatment, only 60% of mice given poly I:C had developed tumors and a similar percentage of interferon-treated mice had developed tumors. Milk samples from mice in all 4 treatment groups were positive for mammary tumor virus.

- 2347 DISTRIBUTION OF VIRAL ANTIGEN IN MOUSE MAMMARY TUMOR CELLS AS REVEALED BY FERRITIN ANTIBODY CONJUGATE TECHNIQUE. (E.) Okano, H. (Fac. Med., Kyushu U., Fukuoka, Japan). *Acta Path Jap* 21(1):57-66, 1971.

Type B virus particles were isolated from a spontaneous C3H mouse mammary carcinoma and used to inoculate male rabbits for the purpose of obtaining an antiserum against the B type particles. The antiserum was conjugated with ferritin and allowed to penetrate frozen slices of mouse mammary tumor, which contained A virus particles as well as B particles. Ferritin granules were found deposited on type B particles and on budding A particles; some ferritin granules were seen on the naked cytoplasmic A particles. On the basis of the localization of the ferritin granules, it was thought that type A virus particles and type B particles share some antigenic property.

- 2348 STUDIES ON MICE OF A TUMOR RESISTANT STRAIN (X/Gf): VIII. TYPE C PARTICLES IN MAMMARY TUMORS OF FRIEND LEUKEMIA VIRUS-INFECTED MICE. (E.) Goldfeder, A. (The Mount Sinai School of Med. of the City U. of New York, New York), E. de Harven and C. Friend. *Rev Europ Etud Clin Biol* 16(4):323-328, 1971.

Mice of strain X/Gf, which do not develop spontaneous neoplasms and which are resistant to tumor induction by irradiation, were infected with Friend leukemia virus at different ages. Eight of 11 mice infected before 3 wk of age developed leukemia, while only 5 of 15 mice infected at more advanced ages developed leukemia. Mice surviving the initial virus infection were divided into 2 groups: one group was given 400 r of X-irradiation at intervals of 53-103 days after virus infection while the other group was not given X-irradiation. Mice in the irradiated and virus-infected group developed malignant lymphoma and lymphatic leukemia in some cases, while mice infected with virus but not given X-irradiation developed malignant lymphoma, reticulum cell sarcoma, and in some cases hepatoma. Two female mice

treated with both radiation and virus infection developed mammary adenocarcinoma. Mammary tumors were found to contain C type virus particles similar to particles associated with murine leukemia.

- 2349 ANTIGENICALLY DISTINCT FORMS OF MAMMARY TUMOR VIRUS IN BLOOD AND MAMMARY TISSUE OF MICE. (E.) Nandi, S. (Dept. Zool., U. Calif. Berkeley), S. Haslam and C. D. Aldrich. *J Natl Cancer Inst* 46(5):1035-1038, 1971.

Mammary tumor virus (MTV) antigens from mammary tissue or milk from BALB/cfC3H/Crg1 (C⁺) mice with Freund's adjuvant were used to immunize syngeneic adult female C⁺ mice and New Zealand White rabbits by i.p. injection on day 1 and without adjuvant on days 30 and 68. The mice were bled on day 90 and pooled sera from 3 separate sets of rabbits were heat-inactivated by incubation at 56°C for 30 min subsequently adsorbed *in vitro* with RBC from MTV- (C⁻) mice. Both mouse and rabbit antisera against MTV neutralized mouse MTV but not rabbit MTV. Of mice injected with virus incubated with antiserum against B particles and tumor extracts from C⁺ mice 7% developed an average of 2 nodules per mouse, whereas 34 of 39 mice, or 87% developed an average of 19 nodules in the control groups. In contrast rabbit MTV incubated in the same antisera induced an average of 31 nodules per mouse among 26 of 37 mice or 70% compared to an average of 25 nodules among 27 control mice, or 63%. Results indicate that MTV activity in mammary tissue extracts, but not hemolyzed RBC preparations, can be neutralized by syngeneic or allogeneic mouse or rabbit antisera against virus preparations from milk or mammary tumors.

- 2350 DEMONSTRATION OF DIFFERENCES IN MURINE SARCOMA VIRUS FOCI FORMED IN MOUSE AND CELLS UNDER A SOFT AGAR OVERLAY. (E.) Levy, J. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *J Natl Cancer Inst* 46(5):1001-1006, 1971.

Cultures of mouse embryo cells and rat kidney cells were infected on soft agar overlay media with murine sarcoma virus. In the mouse cells, the virus produced foci of infection which released both murine sarcoma virus and murine leukemia virus; however transformed mouse cells could not be subcultured. Foci of virus infection in rat cells generally did not yield either sarcoma virus or leukemia virus unless the cultures were superinfected with leukemia virus. Foci in rat cells could be subcultured.

- 2351 *IN VIVO* ENHANCEMENT OF A MURINE SARCOMA VIRUS BY DIETHYLAMINOETHYL-DEXTRAN. (E.) Gazdar, A. F. (Nat. Cancer Inst., Nat. Inst. Hlth., Bethesda, Md.), E. Russell and R. H. Bassin. *Proc Soc Exp Biol Med* 137(1):310-314, 1971.

Mice of the NIH Swiss strain were administered injections of DEAE-dextran in association with inoculations of Moloney murine sarcoma virus (MSV) and

effect of the DEAE-dextran treatment on the tumorigenicity of the virus inoculum was observed. When 200 µg of DEAE-dextran was inoculated together with the virus, the latency period for tumor appearance was shortened; in addition a 10-fold enhancement was seen in the minimal dose of virus required to induce tumors. DEAE-dextran-treatment reduced the number of regressing tumors developed by treated mice. When mice were given 200 µg DEAE-dextran 1 hr before inoculation with virus, pretreated mice developed tumors earlier than did mice not treated with DEAE-dextran. Pretreated mice developed tumors earlier than did mice given DEAE-dextran and virus simultaneously; latent periods for the 2 groups were 6.4 and 8.1 days, resp. The addition of a murine leukemia virus helper virus to the MSV did not affect the latency for virus-induced tumor development, with or without DEAE-dextran treatment.

2352 COMMON GENETIC ALTERATIONS OF RNA TUMOUR VIRUSES GROWN IN HUMAN CELLS. (E.)

Aaronson, S. A. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *Nature* 230(5294):445-447, 1971.

Factors contributing to the occurrence of host range alterations in murine sarcoma viruses grown in human cell cultures were investigated. A human fibroblast strain derived from a skin biopsy of a healthy subject, BALB/3T3 and NIH/3T3 mouse cell lines and normal rat kidney (NRK) cell lines were subjected to transformation by purified strains of Kirsten murine sarcoma virus (KiMuSV/KiMuLV) or Rouschke murine leukemia virus (R-MuLV). The Kirsten virus consisted of 2 strains, one transforming (KiMuSV) and one non-focus-forming helper murine leukemia virus (KiMuLV). All transformed cell lines were propagated through 4-16 generations. After continued cell passages for several wk the released sarcoma viruses lost their ability to transform mouse NIH/3T3 cells and virus replication became more intense in human cells; equal focus inducing capability in human fibroblasts and in NRK cells was then observed. No change in host range could be noticed when KiMuSV/KiMuLV was grown in either NRK or NIH/3T3 cells for long periods. Further tests indicated that both the sarcoma and leukemia viruses of the Kirsten group had undergone a genetic modification during their growth in human cells. However, human or NRK cells infected with either of the altered viruses developed murine viral group specific antigens detectable by complement fixation indicating that these viruses maintained their murine character. Neutralization studies with each of the genetically altered viruses revealed that antisera against human R-MuLV or KiMuSV/KiMuLV were potent inhibitors of focus-formation. In contrast, neither antiserum infected the parent virus strain, indicating that common surface antigens not detectable in the original virus stocks existed in the genetically altered viruses.

2353 ISOLATION OF A RAT-TROPIC HELPER VIRUS FROM M-MSV-0 STOCKS. (E.)

Aaronson, S. A. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *Virology* 44(1):29-36, 1971.

A non-focus-forming virus was isolated from the M-MSV-0 strain of rat Moloney murine sarcoma virus grown on normal rat kidney cells; the new virus had properties of a leukemia helper virus. The host range of the new virus was similar to that of M-MSV-0; it transformed rat cells but not mouse cells; furthermore, the new virus could be neutralized by antiserum to M-MSV-0. The new virus was able to transform normal rat kidney cells in the absence of leukemia virus but was unable to produce detectable virus or viral antigens in the absence of leukemia virus. The unusual host range and antigenicity of M-MSV-0 were thought to be expressions of the new virus, and it was suggested that the new virus may be an indigenous virus of the rat.

2354 INDUCTION OF SUGAR UPTAKE BY A HAMSTER PSEUDOTYPE SARCOMA VIRUS. (E.)

Hatanaka, M. (Flow Lab. Inc., Rockville, Md.), R. V. Gilden and G. Kelloff. *Virology* 43(3):734-736, 1971.

Hamster embryo cell cultures were infected with a pseudotype virus having the envelope and internal virion antigens of a hamster C-type virus and the sarcoma genes of the Moloney strain murine sarcoma virus [M-MSV(HaLV)], and the rate of sugar uptake by the cultured cells was determined. Secondary cultures of hamster embryo cells were inoculated with M-MSV(HaLV) and HaLV helper virus. A greatly enhanced rate of ^{14}C -D-glucose was observed in the sarcoma virus-infected cells compared to non-infected controls or helper virus-infected cells. The enhanced uptake occurred along with the first appearance of morphologically altered cells and seemed to be dependent on the actual transformation process. Cells infected with helper virus became resistant to superinfection with sarcoma virus at 7 days and were actively producing virus as revealed by uridine labeling and density gradient studies. Determination of the kinetic constants for glucose uptake showed an approximate 10-fold decrease in K_m for infected cultures without a similar dramatic change in V_{max} . The induction of sugar uptake parallels that seen in mouse cells infected with murine sarcoma viruses, suggesting that the sarcoma genes in the hamster pseudotype virus are responsible for the enhanced sugar uptake.

2355 VIRUS SPECIFIC RNA IN CELLS TRANSFORMED BY RNA TUMOUR VIRUSES. (E.)

Green, M. (Saint Louis U. Sch. Med., Mo.), H. Rokutanda and M. Rokutanda. *Nature* 230(16):229-232, 1971.

Highly radioactive Harvey murine sarcoma virus (MSV-H) ^3H -DNA was annealed with RNA from MSV-H transformed mouse cells (MEH cell line) or with RNA from normal mouse cells; the amount of product was measured by cesium sulfate density gradient centrifugation and by chromatography. Seventy percent of the DNA label from transformed cells was found in the hybrid position, demonstrating the presence of virus specific RNA, while no hybrid was seen in control cells. Hydroxyapatite chromatography revealed that 12-73% of hybrids were formed from nuclear RNA and that about 14-56% of hybrids were formed from cytoplasmic

(S-30) RNA, compared to values of 15-65% from nuclear RNA and 37-53% from cytoplasmic RNA with the use of cesium sulfate gradients; more hybrids were formed with larger concentrations of RNA. Cells cryptically transformed by RNA tumor viruses which contain no detectable infectious virus, gave a maximum hybrid yield of 30% compared to the maximum 73% yield in transformed cells that replicate virus.

- 2356 ANTIGENIC DIFFERENTIATION OF M-MSV(0) FROM MOUSE, HAMSTER, AND CAT C-TYPE VIRUSES. (E.) Gilden, R. V. (Flow Lab. Inc., Rockville, Md.), S. Oroszlan and R. J. Huebner. *Virology* 43(3):722-724, 1971.

A virus isolated from a female BN rat inoculated with the Moloney strain of murine sarcoma virus was analyzed antigenically in complement-fixation and gel diffusion assays with guinea pig antiserum for the mouse and hamster major group-specific determinants and with dog serum having anti-gs-1 antigen of feline C-type viruses. Positive fixation was not seen at a 1:4 dilution with guinea pig and dog sera containing gs-1 antibodies; negative results were also obtained with gel diffusion. Serum pool obtained from rats immunized with murine sarcoma virus transplant tumors readily detected the common antigen in the virus isolated from the rats and other C-type preparations.

- 2357 DEOXYRIBONUCLEIC ACID POLYMERASE OF ROUS SARCOMA VIRUS: STUDIES ON THE MECHANISM OF DOUBLE-STRANDED DEOXYRIBONUCLEIC ACID SYNTHESIS. (E.) Faras, A. (Dept. Microbiology, U. California, San Francisco), L. Fanshier, A.-C. Garapin, W. Levinson and J. M. Bishop. *J Virol* 7(5):539-548, 1971.

The mechanism of DNA synthesis *in vitro* by Rous sarcoma virus polymerase was examined. A preliminary model was established which included 4 basic features of the reaction so far elucidated. The initial event consists of the formation of a DNA:RNA hybrid in which short segments of single-stranded DNA are synthesized utilizing 70S RNA as template. DNA contained in this hybrid is partially accessible to digestion by a single strand-specific endonuclease indicating that the hybrid possesses branches of single-stranded DNA. This single-stranded DNA serves as a template and precursor for the synthesis of double-stranded DNA. The synthesis of double-stranded DNA appears to occur in association with viral RNA. Double-stranded DNA could not be formed until after its release from the hybrid. Disruption of the hybrid by hydrolysis with RNase in low concentrations of electrolytes resulted in the partial isolation of single-stranded DNA. Synthesis of DNA seems to be effected by an undisturbed series of enzymatic reactions which may approximate the circumstances that follow viral infection.

- 2358 COMPARISON OF ROUS SARCOMA VIRUS-SPECIFIC DEOXYRIBONUCLEIC ACID POLYMERASES IN VIRIONS OF ROUS SARCOMA VIRUS AND IN ROUS SARCOMA VIRUS-INFECTED CHICKEN CELLS. (E.) Coffin, J. M. (McArdle Lab., U. Wisconsin, Madison) and H. M. Temin. *J Virol* 7(5):625-634, 1971.

Chick embryo fibroblasts were infected with Rous sarcoma virus, and infected cultures were labeled with ^3H -uridine or ^3H -leucine; virus was harvested from cultures and virion cores were prepared by disruption of viruses. When virions were examined on sucrose density gradients, a core fraction was found which had a density of approximately 1.24. This fraction contained all of the uridine label about a third of the leucine label. Endogenous viral DNA polymerase activity was confined to the density fraction. Both RNA and DNA dependent DNA polymerases were found at the top of the density gradients. When Rous virus-infected chicken cells were subjected to density gradient centrifugation, RNA and DNA dependent DNA polymerase were present in infected cells. These polymerases were also found in particles released from disrupted infected cells; these particles contained viral RNA and had densities greater than 1.30 g/cc.

- 2359 TRANSFORMATION BY ROUS SARCOMA VIRUS: EFFECTS ON CELLULAR GLYCOLIPIDS. (E.) Hakomori, S.-I. (Dept. Pathobiol., U. Washington Med., Seattle), T. Saito and P. K. Vogt. *Virology* 44(3):609-621, 1971.

Four kinds of sialosylglycolipids, 1 neutral glycolipid and a ceramide were found in chick embryo fibroblast cell cultures. The sialosylglycolipids included hematoside (SL-1), disialosylhematoside (SL-2), monosialosyl glycolipid mixture (SL-3) and disialosyl glycolipid mixture (SL-4). Chick embryo fibroblast cells were infected with Rous sarcoma viruses, including Schmidt-Ruppin Rous virus, Rous associated virus and Prague strain Rous virus. It was found that the SL-2 and SL-3 contents decreased drastically in cells infected with Prague strain Rous virus or with a pseudotype of fusiform Rous virus, while the contents of ceramide and neutral glycolipid usually increased by more than 100%. In chick embryo fibroblast cultures infected by Rous associated virus, little change was seen in the cellular glycolipid contents. Turnover rates for SL-1, SL-2 and SL-3 were accelerated in cell cultures transformed by Prague strain virus and pseudotype Rous virus; cell cultures infected by Rous-associated virus did not show an appreciable change in rate of glycolipid turnover relative to the rates for uninfected control cultures.

- 2360 SUBCUTANEOUS TUMOURS INDUCED BY BRYAN STRAIN CHICKEN ROUS SARCOMA IN THYMECTOMIZED AND ALS-TREATED HAMSTERS. (E.) de Haller, F. (Cancer Inst., U. Louvain, Belgium). *Neoplasia* 18(1):33-39, 1971.

ryan strain Rous sarcoma virus derived from chickens was injected s.c. into hamsters less than 1 day of age; the hamsters were previously thymectomized or given antilymphocyte serum (ALS). In some cases, ALS was administered 7 days after virus inoculation and in some cases ALS was administered prior to virus infection. Virus inocula consisted of 0.2 ml of undiluted virus. None of the control hamsters (no thymectomy and no ALS) developed tumors. However, 100% of the thymectomized hamsters developed tumors within 1 month of inoculation. Tumors were s.c. carcinomas, sometimes fibrosarcomatous, but more often undifferentiated and could be serially transplanted in adult hamsters. Hamsters given ALS 7 days after virus infection did not develop tumors; however, hamsters given ALS prior to virus infection developed tumors in 70% of cases within 10-20 days post-infection. While most of the tumors in the thymectomized group eventually regressed, tumors in the ALS group contained high titers of virus and often progressed, causing death.

361 REVERSION IN VIRUS-TRANSFORMED CELLS. (E.) Macpherson, I. (Imperial Cancer Res. Fund, London, England). *Biochem Pharmacol* 20(5):1005-1008, 1971.

The Schmidt-Ruppin strain of Rous sarcoma virus was found to transform hamster cells *in vitro*, but a few cell colonies among the transformed cells retained the characteristics of the untransformed line (revertant cells). Revertant cells in these cultures apparently did not possess the viral genome; transformed cells showed high colony-forming efficiency, induced tumors in hamsters, and contained an avian leukosis virus-group specific antigen. Virus could be recovered from transformed cells. By contrast, revertant cells had minimal colony-forming efficiency, were only slightly effective in inducing tumors in hamsters and lacked the group specific antigen. Revertant cells did not permit the recovery of virus. While hamster cells infected with Rous sarcoma virus produced revertant cells spontaneously, hamster cells infected with and transformed by polyoma virus did not; nevertheless, revertant cells appeared in polyoma virus-transformed cultures following the induction of chromosome loss from a line of nearly triploid hamster cells transformed by polyoma. Both revertant Rous sarcoma virus-transformed cells and revertant polyoma virus-transformed cells could be retransformed by the respective viruses.

362 NATURE OF RIBONUCLEASE-RESISTANT NUCLEIC ACID OF CHICK EMBRYO CELLS TRANSFORMED BY SCHMIDT-RUPPIN STRAIN OF ROUS SARCOMA VIRUS. (E.) Borelli, K. K. (Rockefeller U., New York, N. Y.). *Nature* 229(1):25-27, 1971.

The mode of replication of oncogenic viral RNAs was studied by investigating the presence of RNase-resistant RNA structures in chick embryo cells transformed by Schmidt-Ruppin Rous sarcoma virus (SR-RSV). The RNase-resistant nucleic acid isolate (peak I NA) had an absorption maximum at 258 nm and a minimum at

230 nm and a ratio of light absorption at 280 nm/260 nm of 0.5. The total radioactivity ($5\text{-}^3\text{H}$ -uridine) of this material constituted approximately 0.54% of the total radioactivity of the cellular nucleic acids. Peak I NA was not affected by the combined actions of RNase A and RNase T₁ or by normal NaOH; however, it was rendered acid-soluble by prolonged digestion (4 hr) with pancreatic DNase at 37°C in a Tris-HCl (pH 7.45) buffer. When peak I NA was hydrolysed and its purines and pyrimidines separated, 97% of the radioactivity appeared to be associated with cytosine and only 0.4% with uracil. When subjected to equilibrium density centrifugation in CsCl solution, the nucleic acid banded at a density of 1.695 g/ml. Peak I NA contained 17.2 guanine, 28.9 adenine, 24.9 cytosine and 29.0 thymine (moles %), when purified by centrifugation in CsCl solution; it contained no uracil, and its base composition was similar to that of healthy chick embryo cellular DNA. The radioactive cytosine from peak I NA must have been derived from $5\text{-}^3\text{H}$ -uridine. The resistance of peak I NA to NaOH, its susceptibility to DNase and the conversion of $5\text{-}^3\text{H}$ -uridine to the cytosine moiety suggest no evidence for the existence of RNase-resistant RNA in chick embryo cells transformed by SR-RSV; the RNase-resistant NA of peak I material apparently was DNA.

2363 FURTHER STUDIES ON MAMMALIAN CELL STRAINS TRANSFORMED BY AVIAN SARCOMA VIRUSES. (E.) Smidova, V. (Slovak Acad. Sci., Bratislava, Czechoslovakia) and J. Smida. *Neoplasma* 17(6):595-600, 1970.

Avian sarcoma virus strains such as the Schmidt-Ruppin strain of the Rous sarcoma virus (SR-RSV), B77V, the Fujinami sarcoma virus (FSV) and the Bryan standard RSV (BS-RSV) were used to investigate the oncogenicity and the presence of viral genome in transformed mammalian (rat embryo) cells after cloning. Two cell strains, B77R and PB, were established following transformation *in vitro* with B77Y; cell strain SR was established following transformation with SR-RSV, while the FR strain was obtained by transformation with FSV. The B77R and SR cell strains contained the viral genome specified by B77V and SR-RSV. The 2 other cell strains (PB and FR) appeared to be oncogenic for rats and did not contain the viral genome. Oncogenicity and the presence of the viral genome as well as the morphology and growth pattern of the transformed cells remained unaltered upon long-term cultivation *in vitro*. Clonal cell lines from the B77R and SR cell strains proved to have the same features. B77V and SR-RSV could be rescued from B77R and SR clones by intracerebral inoculation into 1-day-old chicks; they showed the same host range in ducklings and Japanese quail as the original viral strain. No virus reproduction in the B77R and SR cell strains could be induced.

2364 BHK CELLS DOUBLY TRANSFORMED BY ROUS VIRUS AND POLYOMA VIRUS: KARYOLOGICAL STUDY. (E.) Berebbi, M. (Regional Anti-Cancer Ctr.,

Marseille, France) and H. Bonneau. *Rev Europ Etud Clin Biol* 16(3):246-250, 1971.

Karyological studies were performed on normal baby hamster kidney fibroblasts (strain BHK 21/13), on BHK 21/13 cells transformed by Rous sarcoma virus (Bryan strain), on BHK 21/13 cells transformed by the polyoma virus, on BHK 21/13 cells transformed by Rous sarcoma virus (Schmidt-Ruppin strain) and polyoma virus, on BHK 21/13 cells transformed by Rous sarcoma virus (Bryan strain) and polyoma virus, and on BHK 21/13 cells transformed by Rous sarcoma virus (Bryan strain) and irradiated polyoma virus. Normal BHK 21/13 cells and polyoma virus-transformed cells had a modal chromosome number of 44; however, cells transformed by Rous sarcoma virus (Bryan strain) were hypotetraploid. All clones of cells transformed by Rous virus as well as by polyoma virus were diploid or pseudodiploid in chromosomal mode. A subline of BHK 21/13 cells transformed by Rous virus and irradiated polyoma virus was hypotetraploid, having a mode of 70-72 chromosomes. No specific chromosomal structural anomalies were found to be induced in BHK 21/13 cells transformed by Rous sarcoma virus and/or polyoma virus; however, marker chromosomes were found in the cells transformed by the irradiated polyoma virus.

- 2365 ONCOGENICITY OF THE RIBONUCLEIC ACID EXTRACTED FROM CHICKEN SARCOMA INDUCED BY THE CARR (ZILBER) STRAIN OF ROUS SARCOMA VIRUS (RSV-CARR/ZILBER/-RNA) IN MICE. (Fr.) Nastac, E. (Acad. Med. Sci., Bucharest, Rumania), M. Lungu, P. Athanasiu and M. Stoian. *Ann Histochem* 15(4): 273-282, 1971.

RNA, extracted from a chicken sarcoma induced by the Carr (Zilber) strain of Rous sarcoma virus (RNA Carr RSV), was inoculated into randombred white mice to test its oncogenicity in mammals. A phenolic extract containing 200-300 µg/ml RNA was given to newborn mice (0.2 ml s.c.), to pregnant mice during the last 4 days of pregnancy (0.5 ml i.p.), and to adult mice (s.c. or intracerebrally). Similar groups were inoculated with an RNase-treated (10 µg/ml for 30 min at 37°C) RNA extract (negative control) or with a suspension of avian tumor cells (ATC) at a 1:20 dilution (positive control). The mice treated with RNA Carr RSV or ATC developed generalized adenoid hypertrophy, solid tumors of the lung or considerable hepatosplenomegaly; RNase-treated extracts did not show any oncogenicity. The induced neoplasia was transmissible in both cases (2-4 passages). Microscopy revealed intense proliferation of the alveolar epithelium and infiltration of lymphoblastic cells in the lung, diffuse infiltration of the sinusoidal spaces with lymphoblasts and dystrophic alterations of the hepatocytes in the liver, and a considerable lymphoid proliferation within the adenoid and spleen tissues. The i.m. inoculation of tumor cell suspensions from these mice to 3-wk-old white leghorn chickens induced sarcomas typical for the RSV strain used in the experiment.

- 2366 RELATIONSHIP BETWEEN INITIATING DOSE AND CONCENTRATION OF ROUS SARCOMA VIRUS (TYPE 0) IN TUMORS OF GERM-FREE QUAIL. (E.) Bryan, W. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda Md.), M. R. Sacksteder, R. D. Schwartz, J. P. Kvedar, P. K. Vogt and J. Warren. *J Nat Cancer Inst* 46(5):1093-1097, 1971.

Germ-free Japanese quail 20-40-days-old were inoculated with Rous sarcoma virus type 0 (RSV(0)) derived from chick embryo fibroblasts originally infected with chick tumor extracts. Virus dilutions of 10^{-5} produced a sarcoma incidence of less than 25% in inoculated birds, while dilutions of 10^{-3} to 10^0 produced 100% tumor incidence. A correlation was found between the tumor incidence produced by various virus dilutions and the log titer of virus recoverable from tumors. Virus dilutions of 10^{-5} produced log titers of less than 2.0 of recoverable virus, while dilutions of 10^{-2} to 10^0 produced log titers of 6-7. Plasma of chicks bearing tumors induced by RSV(0) were free of neutralizing antibody against that virus.

- 2367 COMPARATIVE STUDY OF ROUS VIRUS VARIANTS ISOLATED FROM MURINE ROUS SARCOMAS AND THE ORIGINAL CARR-ZILBER STRAIN. (Rus.) Kryukov, I. N. (N. F. Gamalaya Inst. Epidem. Microbiol. Acad. Med. Sci., U.S.S.R., Moscow), I. B. Obukh and F. Tot. *Vop Virus* 16(1):92-97, 1971.

Syngeneic mouse embryo cells were infected by but not transformed by Rous virus-induced tumors when inoculated into adult mice. The Rous virus variants isolated from these tumors differed from the original Carr-Zilber strain in their oncogenicity for adult mice and in their decreased capacity to produce transformation foci in chick embryo chorioallantoic membranes (CAM), regardless of the presence or absence of antigens belonging to the original strain as shown by cross neutralization tests. The investigated Rous virus variants (K-3, Af₁₃, IaAf, Af₂₅, SHC₃H, CC₅₇Br, C₃H) produced transformation foci with characteristic morphology in CAM; the virus isolated from the foci appeared to be oncogenic in adult mice. The original Carr-Zilber strain also acquired carcinogenicity for adult mice following passage on CAM.

- 2368 DNA LIGASE AND EXONUCLEASE ACTIVITIES IN VIRIONS OF ROUS SARCOMA VIRUS. (E.) Mizutani, S. (McArdle Lab. Cancer Res., U. Wisconsin-Madison), H. M. Temin, M. Kodama and R. T. Wells. *Nature* 230(16):232-235, 1971.

Incubation of disrupted virions of Schmidt-Ruppin avian sarcoma virus with 32 P-poly d(IC)-d(IC) resulted in a decrease in the amount of acid insoluble 32 P in the absence of bacterial alkaline phosphatase; subsequent incubation of the virions with 5 mM phosphatase did not inhibit this reaction. Chromatography of the products of the reaction showed that both 5'-dIMP and 5'-dCMP were formed. Exonuclease activity

was demonstrated to be dependent upon divalent cations and was inactivated by heating; no inhibition was seen with P-chloromercuribenzoate. An increase in bacterial alkaline phosphatase resistant ^{32}P was found with time; the reaction was roughly proportional to the amount of disrupted virions in the reaction mixture, was dependent upon the presence of a divalent cation and showed greater activity in the presence of manganese than in magnesium. The ^{32}P product of the ligase reaction was hydrolyzed either by micrococcal nuclease and spleen phosphodiesterase or by pancreatic DNAase I and venom phosphodiesterase.

- 2369 STRUCTURAL POLYPEPTIDES OF SIMIAN VIRUS 40. (E.) Estes, M. K. (School Med., U. North Carolina, Chapel Hill), E.-S. Huang and J. S. Pagano. *J Virol* 7(5):635-641, 1971.

Simian virus 40 (SV40) was grown in animal cells and purified prior to analysis by electrophoresis on polyacrylamide gels containing sodium dodecyl sulfate (SDS). The purified virus was seen to contain 6 virion proteins (VP1-6) with molecular weights ranging from 11,000-43,000. VP1 had a molecular weight of 43,000 and contained 70% of the virus protein, VP2 had a molecular weight of 32,000 and contained 9% of the virus protein, VP3 had a molecular weight of 23,000 and contained 10% of the virus protein, VP4 had a molecular weight of 14,000 and contained 6% of the virus protein, VP5 had a molecular weight of 12,500 and contained 4% of the virus protein, and VP6 had a molecular weight of 11,000 and contained 3% of the virus protein. Empty virions contained reduced amounts of VP4, 5 and 6. On velocity centrifugation of degraded SV40, VP1 and VP2 remained at the top of the centrifuge gradient, while VP4, 5 and 6 sedimented as a complex with the viral DNA. VP3 was found in association with VP1 or with the smaller polypeptides. It was thought that the latter formed the nucleoprotein of the SV40 virion, and that VP1 and VP2, which comprised about 80% of the virus protein, formed the virus capsid. VP3 may have represented an intermediate component.

- 2370 INDUCTION OF CELL DIVISION IN MEDIUM LACKING SERUM GROWTH FACTOR BY SV40. (E.) Smith, J. S. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), C. D. Scher and G. J. Todaro. *Virology* 44(2):359-370, 1971.

BALB/3T3 mouse cells were infected with SV40; the cells had been grown in a culture medium which lacked protein growth factors necessary for cell division. Despite the lack of growth factors, SV40 infection induced cell division in the mouse cells; by 5 days after infection, colonies containing 8 or more cells were seen in infected cultures. The number of cell divisions induced in infected cultures was proportional to the input multiplicity of virus infection. When SV40 was exposed to an infectivity-inhibiting dose of UV, the capacity of virus to produce growth in the factor-free medium was reduced,

which suggested that the viral genome was needed to induce cell division. Transformation by SV40 of cells in factor-free medium was apparently not permanent; 36 of 57 colonies induced to divide by SV40 did not contain SV40 T antigen. In addition, few of the SV40-transformed cells grew to high saturation density when shifted to a complete growth medium. One SV40-transformed clone which was able to grow in factor-free medium displayed strong contact inhibition despite its production of SV40 T antigen.

- 2371 STUDIES OF NONDEFECTIVE ADENOVIRUS 2-SIMIAN VIRUS 40 HYBRID VIRUSES: II. RELATIONSHIP OF ADENOVIRUS 2 DEOXYRIBONUCLEIC ACID AND SIMIAN VIRUS 40 DEOXYRIBONUCLEIC ACID IN THE $\text{Ad2}^+\text{ND}_1$ GENOME. (E.) Levin, M. J. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), C. S. Crumpacker, A. M. Lewis, Jr., M. N. Oxman, P. H. Henry and W. P. Rowe. *J Virol* 7(3):343-351, 1971.

A hybrid virus which was able to replicate without the presence of a nonhybrid adenovirus helper was isolated from an adenovirus 2-SV40 hybrid population; the nondefective adenovirus was designated $\text{Ad2}^+\text{ND}_1$. The DNA from $\text{Ad2}^+\text{ND}_1$ was obtained free of nonhybrid adenovirus DNA and was shown by RNA-DNA hybridization tests to consist of nucleotide sequences which were complementary to adenovirus 2 and to SV40-specific RNA. Equilibrium density and rate zonal centrifugation indicated that these nucleotide sequences were linked together in the same DNA molecules by alkali-resistant bonds. It was estimated that about 1% of the $\text{Ad2}^+\text{ND}_1$ DNA consisted of SV40 nucleotides.

- 2372 MALIGNANT TRANSFORMATION *IN VITRO* BY "NON-ONCOGENIC" VARIANTS OF DEFECTIVE SV40 (PARA). (E.) Butel, J. S. (Baylor Coll. Med., Houston, Texas), S. S. Tevethia and M. Nachtigal. *J Immunol* 106(4):969-974, 1971.

Lung and kidney cells from weanling male Syrian hamsters of the LSH/ssLAK inbred strain were found to undergo transformation *in vitro* when inoculated with 4 variants of the PARA (defective SV40)-adenovirus that was "non-oncogenic" for newborn hamsters *in vivo*. The multiplicity of infection ranged from 1.3 to 9 plaque-forming units with latency periods ranging from 2 to 7 wk. The cell lines transformed by the non-oncogenic variants of PARA could not be distinguished in tissue culture from those transformed by oncogenic viruses and were found to contain SV40 T and S antigens upon immunofluorescence testing. Transplantability of these cells into syngeneic weanling hamsters at concentrations of 10^6 or 10^5 cells/animal varied; most of the transformed lung cells induced tumors *in vivo* with latency periods ranging between 4-10 wk except for one cell line that produced tumors in 1 of 10 hamsters 14 wk after inoculation. The transformed kidney cell lines elicited a wide spectrum of transplantability, and it was not possible to conclude whether lung or kidney cells are better indicators

of the oncogenic potential of PARA-adenoviruses. All the cell lines established following transformation by oncogenic variants of PARA were readily transplantable *in vivo*. Sera collected from hamsters bearing tumors induced by the defective para-transformed cell lines contained antibody against adeno T antigens in 16 of 35 cases and antibody against SV40 T antigens in 28 of 35 cases.

- 2373 QUANTITATION OF SIMIAN VIRUS 40 SEQUENCES IN AFRICAN GREEN MONKEY, MOUSE, AND VIRUS-TRANSFORMED CELL GENOMES. (E.) Gelb, L. D. (Natl. Inst. Allergy and Infectious Dis., Natl. Inst. Hlth., Bethesda, Md.), D. E. Kohne and M. A. Marten. *J Mol Biol* 57(1):129-145, 1971.

Simian virus 40 (SV40) DNA prepared from infected African green monkey kidney, BSC-1 or Vero cells, DNA from homogenates of normal green monkey, 3T3 and hamster SV40 tumor cell, and salmon sperm DNA were used to study hybridization and re-association kinetics. No significant reaction occurred between labeled SV40 DNA and the immobilized green monkey DNA. In 4 of the 5 SV40-transformed lines examined, the SV40 genome equivalents per mammalian diploid cell ranged from 1.04-3.86, with the large value present in only 1 line.

- 2374 SV 40 VIRUS TRANSFORMED PROSTATIC CARCINOMA IN THE HAMSTER: II. COMPARISONS OF LACTATE DEHYDROGENASE ISOENZYMES WITH HUMAN PROSTATIC CANCER. (E.) Abdalla, A. M. (Roy. Victoria Hosp., Montreal, Quebec, Canada) and J. A. Oliver. *Invest Urol* 8(5):488-493, 1971.

The electrophoretic mobility patterns of the lactate dehydrogenase isoenzyme (LDH) of an SV40-induced hamster prostatic carcinoma and of a human prostatic carcinoma were compared. Tumor tissues and serum samples from hamster and human were prepared by centrifugation and subject to electrophoresis on agarose gel. Both human and hamster tumor tissue showed 5 distinct fluorescent areas of electrophoretic activity. Whereas in human prostatic carcinoma, the fifth fraction of LDH migrated toward the cathode, thus indicating that it is positively charged, the fifth fraction of LDH in the hamster tumor migrated toward the anode, thus indicating that it is negatively charged.

- 2375 SUSCEPTIBILITY OF TRISOMIC AND OF TRIPLOID HUMAN FIBROBLASTS TO SIMIAN VIRUS 40 (SV40). (E.) Payne, R. E. (Sch. Pub. Hlth., U. Michigan, Ann Arbor) and R. D. Schmickel. *Nature* 230(14):190, 1971.

Fibroblast cultures from human subjects were infected with SV40; triploid human cells (69 XXY), human cells with G trisomy, cells from patients with Fanconi's anemia and normal cells were studied. The susceptibility of the fibroblasts was measured by the proportion of cells producing SV40 T antigen. Among normal

cells, 8.8% produced T antigen and among Fanconi's anemic cells, 39.8% produced T antigen. Among triploid human cells, 8.8% produced viral T antigen and among G-trisomic human cells, 18.1% produced T antigen, suggesting that the increased viral susceptibility of trisomic cells results from factors other than the mere presence of an extra chromosome.

- 2376 INCREASED TRANSFORMATION EFFICIENCY OF SIMIAN VIRUS 40 IN RAT EMBRYO CELLS INFECTED WITH RAUSCHER LEUKAEMIA VIRUS. (E.) Rhim, J. S. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), C. Greenawalt, K. K. Takemoto and R. J. Huebner. *Nature* 230(11):81-82, 1971.

Rat embryo cell cultures infected with Rauscher leukemia virus (RLV) and uninfected cultures were infected with SV40 at input multiplicities of 10^5 to $10^{8.2}$ PFU/culture plate. By 24 days after infection, the average number of transformed foci/plate in cultures not infected with RLV ranged between 10-100, while the average number of transformed foci/plate in cultures infected with RLV ranged from 10-110. SV40 tumor antigen was detected in the nuclei of 1-5% of RLV-infected cells and in 1-5% of the nuclei of uninfected cells. The complement fixing antigen titer against murine sarcoma virus rat antiserum was greater than 1:4 in RLV-infected cells and less than 1:4 in uninfected cells.

- 2377 APPARENT DIFFERENCES IN TRANSCRIPTIONAL CONTROL IN CELLS PRODUCTIVELY INFECTED AND TRANSFORMED BY SV40. (E.) Sauer, G. (German Cancer Res. Inst., Heidelberg). *Nature* 231(22):135-138, 1971.

Experiments were carried out to demonstrate the relationship between synthesis of late SV40 mRNA sequences and DNA replication using arabinofuranosylcytosine (ara-C) as an inhibitor of DNA replication. In a hybridization competition experiment, labeled late SV40 mRNA was added to immobilized DNA, and unlabelled SV40 mRNA was included in the reaction mixture in increasing amounts. While late SV40 mRNA extracted 3 hr after infection did not seem to contain SV40-specific sequences, early SV40 mRNA sequences which appeared 6 hr after infection displayed 25% homology with late SV40 mRNA. This homology remained unchanged up to 17 hr after infection. After 19.5 hr new SV40 mRNA sequences were present, which competed with late ^3H -SV40 mRNA. The presence of ara-C in the infected cultures prevented the transcription of new sequences of the viral genome. An experiment to determine whether transcription of early genes was sequential or whether all early genes were being copied simultaneously was performed. It was found that early SV40 genes were transcribed simultaneously during the early period of infection. Ara-C inhibited completely transcription of late SV40 mRNA sequences. It was concluded that DNA replication is a requirement for transcription of late SV40 genes in a productive cycle of infection.

78 DNA REPLICATION IN SV40-INFECTED CELLS:
V. CIRCULAR AND CATENATED OLIGOMERS OF
SV40 DNA. (E.) Jaenisch, R. (Dept. Biochem.,
Princeton U., Princeton, N.J.) and A. Levine.
Virology 44(3):480-493, 1971.

Extracellular viral ^3H -DNA from African monkey
cells infected with simian virus 40 (SV40) was
analyzed by gradient centrifugation and investi-
gated for infectivity. Fraction I sedimented in
alkaline sucrose gradients as a single symmetrical
peak at the position of monomeric SV40 DNA, while
fraction II contained 3 distinct peaks of radio-
activity with the main peak corresponding to the
monomeric viral DNA, 30% sedimenting at a position
expected for double length SV40 DNA, and a third
peak at the position expected for denatured
single-stranded dimers. Fractions III and IV
revealed a considerable amount of monomers, dimers
and other heterogeneous molecules. Electron micro-
scopy revealed circular molecules of various con-
former lengths and various combinations of catenated
molecules; either one or both submolecules were
released by DNase treatment. All fractions were
infectious and the relative infectivity with re-
gard to SV40 DNA (set at 1.0) was 0.5, 0.14, and
0.85 for fractions II', III', IV' (dialyzed
fraction II, III, IV), resp.

79 COMPARISON OF CYTOCIDAL AND NONCYTOCIDAL
STRAINS OF SHOPE RABBIT FIBROMA VIRUS.

(E.) Hinze, H. C. (U. Wisconsin Med. School,
Madison) and D. L. Walker. *J Virol* 7(5):577-581,
1971.

Seven strains of fibroma virus, including Shope
fibroma virus strains 1, 289, 384 and 472, the
original Patuxent strain, the Boerlage strain and
the M1 strain, were used to infect rabbit kidney
cells in culture (1-5 PFU/cell) and the growth of
cells infected with the various virus strains was
compared. All virus strains except M1 produced
similar responses in infected cultures; cell counts
in infected cultures increased from about 10^5 to
about $10^{5.5}$ - $10^{5.7}$ cells/culture within 11 days after
infection. In cultures infected with the M1 virus
strain, cell counts dropped to zero by day 8 post-
infection. The cytotoxic M1 virus strain was found
to differ significantly from a noncytotoxic strain
in rate of virus multiplication, plaque type,
genetic properties or heat lability. Viruses of
various strains produced similar tumors when
injected into rabbits.

80 VIRUS MULTIPLICATION IN CULTURE CELLS SYN-
CHRONIZED BY EXCESS THYMIDINE TREATMENT:
EFFECT OF VIRAL DNA SYNTHESIS OF SHOPE FIBROMA
VIRUS AND COWPOX VIRUS UPON NUCLEAR DNA SYNTHESIS
IN SYNCHRONIZED FL CELLS. (E.) Mantani, M. (Res.
Inst. Microbial Diseases, Osaka U., Japan) and S.
O. *Biken J* 13(4):365-376, 1970.

Cells were synchronized by double excess thymidine
treatment and infected at different stages of the

mitotic cycle with Shope fibroma virus or cowpox
virus; autoradiographic techniques were used to
determine the effect of viral DNA synthesis on
nuclear DNA synthesis in the infected cells. Cellu-
lar DNA synthesis was abolished in cells in which
viral DNA synthesis was going forward in the G_1 phase,
and cellular DNA synthesis was partially inhibited
in cells in which viral DNA synthesis was going for-
ward in the S phase. Both viruses produced similar
effects on cellular DNA synthesis.

2381 ENZYME HISTOCHEMISTRY IN SHOPE PAPILLOMA:
HISTOCHEMICAL OBSERVATIONS OF ENZYMES IN
SHOPE PAPILLOMATOSIS OF THE RABBIT SKIN. (E.) Mori,
M. (Osaka U. Dent. Sch., Japan), M. Morishita, Y.
Yoshimura, T. O. Yoshida and Y. Ito. *Ann Histochem*
15(4):297-310, 1970.

Adult rabbits were infected with Shope papilloma
virus by the scarification method on 8 dorsal sites,
and tissue specimens obtained from hyperplastic skin
and papillomatous growths at the sites of introduc-
tion of the virus were assayed for enzyme activity.
Alkaline phosphatase activity was lacking in normal,
hyperplastic and tumorous epithelium; capillary
vessels, however, were positive for alkaline phos-
phatase. Keratinized regions of infected tissue
were strongly positive for acid phosphatase activity.
Esterase activity was absent in normal epithelium
but present in neoplastic papilloma cells. Amino-
peptidase activity was slight in the stroma of deep
tumors of the dermis. Papillomas and normal tissue
had similar levels of β -glucuronidase. Glucose-6-
phosphatase activity increased during the growth of
papillomas. Succinate dehydrogenase was slight in
papilloma cells, while lactate and glucose-6-
phosphate dehydrogenases were at high levels in
tumor cells.

2382 MULTIPLICATION OF POLYOMA VIRUS IN MOUSE-
HAMSTER SOMATIC HYBRIDS: A HYBRID CELL
LINE WHICH PRODUCES VIRAL PARTICLES CONTAINING PRE-
DOMINANTLY HOST DEOXYRIBONUCLEIC ACID. (E.)
Basilico, C. (New York U. Sch. Med., New York, N. Y.)
and S. J. Burstin. *J Virol* 7(6):802-812, 1971.

When cells of a mouse-hamster somatic hybrid line,
3T3 x BHK (10A), were infected with polyoma virus,
the cells synthesized polyoma virus T antigen, as
did infected 3T3 mouse cells; comparable frequencies
of 10A and 3T3 cells produced virus. However, 10A
cells produced less than 1% of the amount of infec-
tious virus produced by the 3T3 cells. The incor-
poration of ^3H -thymidine into polyoma virus DNA in
10A cells was 5% of that seen in 3T3 cells. Viral
DNA produced in 10A cells was normal in size,
buoyant density and infectivity, but the polyoma
virus particles produced by infected 10A cells were
for the most part noninfectious. The titer of
hemagglutination U in infected 10A cells was
26,000-55,000 U, while titers in infected 3T3 cells
reached 400,000 U. DNA-DNA hybridization experi-
ments indicated that DNA from infected 10A cells
consisted of less than 10% viral DNA and 90%
cellular DNA.

2383 PROPERTIES OF POLYOMA VIRUS TRANSFORMED CELLS: I. ONCOGENIC PROPERTIES. (E.)

Babiuk, L. A. (Dept. Microbiol., U. British Columbia, Vancouver, Canada) and J. B. Hudson. *Canad J Microbiol* 17(6):747-751, 1971.

Three- or 5-wk-old hamsters were given injections s.c. of polyoma virus-transformed hamster cells or polyoma virus itself, and the incidence of tumors produced was observed. It was found that passage of virus-transformed cells *in vivo* resulted in an increase in oncogenicity; the latency of tumor appearance was decreased and as few as 5 or 10 transformed cells were sufficient to produce tumors in hamsters. The time required for induction of tumors following an s.c. dose of transformed cells was directly related to the age of the recipient hamster; tumors appeared 10 days earlier in 3-wk-old animals than in 5-wk-old animals. A direct positive correlation was also seen between number of cells injected and tumor latency. Tumors produced by s.c. injection of virus-transformed cells appeared only at the site of injection and never metastasized. Injections of 10^7 PFU of polyoma virus caused tumors throughout the hamsters. Tumors caused by polyoma virus usually showed more mitotic figures and more anaplastic tissue than did tumors caused by polyoma virus-transformed cells, which were comparatively benign. No oncolytic activity was seen when the arbovirus Powassan was grown in tumor tissue produced by polyoma virus-transformed cells.

2384 INDUCED CELLULAR DNA SYNTHESIS BY 'EARLY' AND 'LATE' TEMPERATURE-SENSITIVE MUTANTS OF POLYOMA VIRUS. (E.) Eckhart, W. (Salk Inst., San Diego, Calif.). *Proc Roy Soc Lond* 177(1046):59-63, 1971.

Mouse embryo fibroblasts were infected with 3 temperature-sensitive mutants of polyoma virus designated ts25, ts238 and ts697; these mutants were able to form plaques at 32° but not at 38°. Fibroblasts were infected at 32° and at 39°. Mutants ts25 and ts697 showed defective DNA synthesis at 39°; the virus yield for ts25 at 39° was 2.5×10^6 and for ts697 it was 5×10^6 ; for ts238, the virus yield at 39° was 1.5×10^7 . Mutants ts25 and ts697 were classified as "early" mutants and ts238 was classified as a "late" mutant. At 32°, ts25 and ts238 showed comparable virus yields and ts697 showed a markedly higher yield. When fibroblasts were infected with a wild-type polyoma virus it was found that the incorporation of ^3H thymidine into cells infected with virus was 2-5 times higher than in mock-infected cells. When fibroblasts were infected with temperature-sensitive polyoma mutants it was found that at 39° the mutants induced DNA synthesis (measured by uptake by infected cells of ^3H thymidine) in infected cells. It was emphasized that the mutants induced cellular DNA synthesis under temperature conditions in which viral gene products were deficient.

2385 PHENOTYPIC VARIATION AND ITS CONTROL IN POLYOMA-TRANSFORMED BHK21 CELLS. (E.)

Wyke, J. (Imperial Cancer Res. Fund, London, England). *Exp Cell Res* 66(1):209-223, 1971.

The 5-bromouracil + blue light selection method was applied to Methocel suspension cultures of polyoma-transformed clones, and variants of Py6/2 proved to be sufficiently stable to grow on soft agar with formation of flat colonies and with very little overlapping. These variants revealed that expression of phenotype in suspensions was reduced to a far greater degree than on a surface. Comparison of clone lines during the first 50 hr of culture showed approximately exponential growth with a mean doubling time of about 15 hr; 2 of the lines showed no sign of degeneration even after 300 hr in the same medium. "Re-transformed" segregants appeared slowly in one variant, but showed rapid appearance in another line. The variants comprised the bulk of the latter population within 30 generations.

2386 THE ANALYSIS OF MALIGNANCY BY CELL FUSION III. HYBRIDS BETWEEN DIPLOID FIBROBLASTS AND OTHER TUMOR CELLS. (E.) Wiener, F. (Karolinska Inst., Stockholm, Sweden), G. Klein and H. Harris. *J Cell Sci* 8(3):681-692, 1971.

Cells of a sarcoma induced by polyoma virus and a spontaneous carcinoma were fused with fibroblasts, mouse embryos and were assayed for tumorigenicity s.c. injection into syngeneic irradiated newborn mice (A.SW×CBA F₁) and allogeneic irradiated newborn mice. In the irradiated syngeneic recipients the wild type population and all clones with reduced chromosome numbers gave take incidences not far from 100%, but 3 of 5 clones that initially showed chromosome complement approximating the sum of the chromosomes of the two parent cells showed a greatly reduced cumulative take incidence. In all cases a range of chromosome numbers seen in the cells of tumors was very much broader than that to be expected from the fusion of one tumor cell with one fibroblast and in almost all cases there was a marked reduction in the modal chromosome number relative to that expected from the fusion. Evidence indicates that generation of malignant variants in the hybrid cell population requires not merely an overall reduction in chromosome number, but the elimination of some specific chromosome or chromosomes derived from non-malignant parent cell.

2387 TRANSFORMATION BY POLYOMA VIRUS AFFECTS ADHESION OF FIBROBLASTS. (E.) Edwards, J. G. (Dept. Cell Biol., U. Glasgow, Scotland), J. A. Campbell and J. F. Williams. *Nature* 231(22):147-148, 1971.

Suspensions of polyoma-transformed cells (Py) derived from clone 13 (C13) of a BHK21 fibroblast culture, unlike C13 cells, elicited decreased aggregation following minimal exposure to trypsin.

(200-300 BAEE U/ml for 3 min at room temperature) and EDTA. While aggregation of Cl3 cells persisted after 11 passages, Py cell lines showed decreased adhesiveness after 8 passages. Aggregation was scarcely detectable in growing Py lines. It is not known whether this decreased adhesiveness in the suspension system is shared by the interaction of the cells in culture and *in vivo*.

2388 SUSCEPTIBILITY TO SUPERINFECTION OF HYBRIDS BETWEEN POLYOMA "TRANSFORMED" BHK AND "NORMAL" 3T3 CELLS. (E.) Basilico, C. (New York U. Med Ctr., New York) and R. Wang. *Nature* 230(12):105-107, 1971.

Somatic hybrid lines were formed by plating C2F, a TK deficient derivative of the 3T3 mouse line which is fully permissive for polyoma multiplication, with one of 2 BHK Polyoma-transformed sublines T6Py5 or T6Py8 (both HGPRT deficient); hybrid cells were selected using medium containing aminopterin, thymidine and hypoxanthine. The transformed hybrids grew in soft agar, synthesized polyoma T antigen, had transformed phenotype morphologically, and exhibited the disordinate growth patterns of transformed cells. No infectious virus was shed by these hybrids nor was it possible to induce virus release by various treatments. All the hybrid lines produced virus when infected, although there was considerable variability in the yield. These experiments indicate that these hybrid cells possess no immunity to superinfection; the permissiveness of these cells to superinfection implies that polyoma-transformed BHK cells do not synthesize a dominant immunity substance with the characteristics of a diffusible viral repressor.

2389 THE ACTION OF POLYOMA VIRUS ON CELL PROLIFERATION *IN VITRO*. (Rus.) Makarova, G. F. N.F. Gamaleya Inst. Epidemiol. Microbiol. Acad. Med. Sci. U.S.S.R., Moscow) and I. S. Irlin. *Vop Virus* 6(1):16-20, 1971.

The mechanism of cell proliferation in polyoma virus-infected mouse and hamster embryo tissue cultures during various stages of growth was investigated *in vitro*. A marked decrease of the mitotic index (from 1.0 to 0.3) and of the labeled cell index (from 18 to 3) along with an increase of the duration of the mitotic cycle (from 20 to 28 hr) and an inhibition of DNA synthesis occurred during the logarithmic stage of growth in the mouse embryo tissue cultures 4 hr following infection. The infection of hamster embryo cells during the same state of growth led to a 10-fold increase of the mitotic index 3 hr following infection and to a stimulation of DNA synthesis. Contact-inhibited cell cultures of both mouse and hamster embryo cell cultures revealed enhanced mitotic indexes and stimulation of DNA synthesis. Parallel determinations of mitotic index and labeled cell index at short time incubation with labeled thymidine revealed the increase of the mitotic index to be preceded by 1 hr by an increase of DNA-producing cells. These results indicated that cells in stage G₂ were also stimulated by infection. Apparently polyoma virus

infection leads to a temporary loss of the contact inhibition control of the investigated cell cultures.

2390 EFFECT OF INTERFERON ON SOME ASPECTS OF TRANSFORMATION BY POLYOMA VIRUS. (E.) Taylor-Papadimitriou, J. (Imperial Cancer Res. Fund Lab., London, England) and M. Stoker. *Nature* 230(12):114-117, 1971.

Interferon inhibited polyoma virus-stimulated DNA synthesis in BHK cells in medium containing only 0.8% serum by 67%; this inhibition was not due to interferon blocking of stable transformation since only 0.03% of serum-deprived cells became stably transformed with the dose of virus used. Interferon had no inhibitory effect on serum-stimulated DNA synthesis. Formation of colonies of 8 cell equivalents or larger in methyl cellulose suspension cultures were inhibited 60-70% by exposure to interferon. The development of random orientation of transformed cells in monolayer cultures in conditions of serum depletion was also inhibited by interferon. The initial development of several characteristics of polyoma-transformed cells seemed to be inhibited by interferon irrespective of whether these characteristics were abortive or stably inherited, although no inhibitory effects were seen once stable transformation was achieved. Stable transformation was thought to involve integration, and an interferon-sensitive viral gene may be required for this event, or integration may modify viral gene products required for the expression of the transformed cell phenotype so that they become insensitive to interferon.

2391 ANTIGENIC HETEROGENEITY IN CELL POPULATIONS OF CLONED POLYOMA, VIRUS-INDUCED TUMOUR LINES. (E.) Negroni, G. (Imp. Cancer Res. Fund, London, England) and E. Hunter. *Nature* 230(9):18-20, 1971.

The variability in malignancy of cells derived from polyoma virus-induced tumors was investigated. Clones of transplantable fibrosarcoma and parotid tumors were derived from C₃H/Bi mice inoculated with polyoma virus. C₃H/Bi mice were immunized by 6 i.p. inoculations each of 1 x 10⁶ transformed non-malignant cells (line 7₂) twice/wk. Both immune and control mice were later inoculated s.c. with 10³-10⁶ malignant cells of fibrosarcoma (line 7₁) or of parotid tumor (line C₄d). The number of cells required to induce tumors in 50% of the preimmunized mice was 10-fold as compared to that required in the controls for both fibrosarcoma and parotid malignant lines. Quantitative comparison of the immune sensitivity of the malignant (7₁, C₄ and C₅) and non-malignant (7₂) cell lines was performed with trypsinized cells mixed with immune serum at 37°C for 1 hr and then with fresh guinea-pig complement for 45 min. The colony forming capacity of cells from this mixture was compared with that of identical cells mixed with normal serum and complement. Kidney cell cultures from 5 day old C₃H/Bi mice or embryo cell cultures from 14-day-old embryos of the same strain were used as controls. No considerable differences

between the number of colonies of control cells treated with normal serum and complement or immune serum and complement were observed. A 100% reduction in the number of colonies occurred when the immune serum (1:2) was mixed with no more than 1×10^5 non-malignant (7_2) cells. Titration of serum activity showed complete inhibition at a 1:16 dilution and a 50% inhibition at a dilution of 1:64 to 1:128. Complement fixing activity tests showed that 1×10^4 non-malignant cells (7_2) absorbed 1 U of complement at a serum dilution of 1:160; 5×10^4 cells of malignant lines 7_1 , C_4 and C_5 absorbed the same amount of complement at a serum dilution of 1:20; control cells (embryo) absorbed no complement. When the colony inhibition test was performed with more than 1×10^5 transformed non-malignant (7_2) cells certain amounts of cells survived the treatment with complement and specific immune serum. Two cell lines could be established *in vitro* from the surviving cell colonies. Cells from 1 of these colonies appeared to be immunosensitive and to produce slow growing tumors in mice. Cells from 3 malignant cell lines (parotid tumor, C_4d and C_5 lines, and fibrosarcoma, line 7_1) were only partially inhibited by specific immune serum and complement. Two subclones (A and B) were established from the 7_1 cell line. Cells of subclone A were not inhibited by specific immune serum and complement; cells of subclone B were moderately inhibited (20%).

2392 THE RECOVERY OF POLYOMA VIRUS FROM INFECTED MOUSE CELLS: RELEVANCE TO VIRUS PURIFICATION. (E.) Kohse, L. M. (Dept. Microbiol, U. British Columbia, Vancouver, Canada), L. McGrath and J. B. Hudson. *Canad J Microbiol* 17(6):775-781, 1971.

2393 VIRUS MULTIPLICATION IN CULTURE CELLS SYNCHRONIZED BY EXCESS THYMIDINE TREATMENT: I. EFFECT OF EXCESS THYMIDINE UPON GROWTH OF POX-VIRUSES AND CHIKUNGUNYA VIRUS. (E.) Mantani, M. (Res. Inst. Microbial Diseases, Osaka U., Japan), Y. Sakaue and S. Kato. *Biken J* 13(4):353-364, 1970.

2394 VIRAL CARCINOGENESIS IN VENEREALLY SUSCEPTIBLE ORGANS. (E.) Ravich, A. (Miami Beach, Fla.). *Cancer* 27(6):1493-1496, 1971.

2395 SEROLOGICAL IDENTIFICATION OF HAMSTER CORNAVIRUSES. (E.) Nowinski, R. C. (Kettering Inst. Cancer Res., New York, N.Y.), L. Old, P. V. O'Donnell and F. K. Sanders. *Nature* (17):282-294, 1971.

2396 CARCINOMA *IN SITU* ASSOCIATED WITH VIRUS CONTAINING ANAL WARTS. (E.) Oriel, J. (St. Thomas' Hosp., London, England) and I. W. V. ster. *Brit J Derm* 84(1):71-73, 1971.

2397 MOSAICS OF CAPSID COMPONENTS PRODUCED BY COCULTIVATION OF CERTAIN HUMAN ADENOVIRUS *IN VITRO*. (E.) Norrby, E. (Karolinska Inst., Stockholm, Sweden) and Y. Gollmar. *Virology* 44(2):383-395, 1971.

2398 DNA POLYMERASE IN DEFECTIVE ROUS SARCOMA VIRUS. (E.) Robinson, W. S. (Stanford Sch. Med., Cal.) and H. L. Robinson. *Virology* (2):457-462, 1971.

2399 LINEAR, SINGLE-STRANDED DEOXYRIBONUCLEIC ACID ISOLATED FROM KILHAM RAT VIRUS. Salzman, L. A. (Natl. Inst. Allergy and Infect. Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, W. L. White and T. Kakefuda. *J Virol* 7(6):830-1971.

2400 RNA SYNTHESIS IN POLYOMA VIRUS-INFECTED MOUSE EMBRYO CELLS IN TISSUE CULTURE. Bowen, J. M. (U. Texas M.D. Anderson Hosp. Tumor Houston), R. G. Hughes, M. D. Scanlon, M. A. Na M. A. Ussery and L. Dmochowski. *Texas Rep Biol* 28(4):519-529, 1970.

See also:

- * (Rev): 2155, 2156, 2157, 2164, 2166, 2168, 2169
- * (Immun): 2409, 2411, 2412, 2413, 2421, 2446, 2447, 2449, 2454, 2455, 2457, 2458, 2463

- 401 ABSENCE OF ENHANCING ANTIBODY IN CELL
MEDIATED IMMUNITY TO TUMOR HETEROGRAFTS
IN PROTEIN DEFICIENT RATS. (E.) Jose, D. G. (Dept.
Med., Variety Club Heart Hosp., Minneapolis, Minn.)
and R. A. Good. *Nature* 231(5301):323-325, 1971.

The cellular and humoral immunity to DBA/2
mouse mastocytoma P-815-X2 ascites tumor
cells was studied in male Charles River rats
subjected to varying degrees of protein-
calorie deprivation which ranged from a low
of 8% casein to a control level of 30% casein.
The diets were started when the animals were
1 wk-old, and at 12 wk a single i.p. immunizing
dose of tumor cells was administered; spleen
cells and serum were obtained from one normal
immunized animal and from matched rats in the
different nutritional groups 11 days after
immunization. Spleen lymphocytes from immuni-
zed animals in all nutritional groups were
most equally active in mastocytoma target
cell lysis. Addition of inactivated serum
from sensitized animals on 30% protein diets
markedly inhibited cell mediated lysis in 7
experiments and showed less than 50% inhibi-
tion in 3 experiments. Serum from sensitized
protein deficient animals showed no inhibition
of cell mediated lysis in any of 10 experiments.
These results indicate that cell mediated immunity
can be maintained and specific antibody blocking
of cellular immunity or enhancing antibody can be
expressed in rats by feeding a diet of 8% casein.

- 402 STUDIES ON THE IMMUNOGENICITY OF PRENEO-
PLASTIC AND NEOPLASTIC MAMMARY TISSUES
IN BALB/c MICE FREE OF THE MAMMARY TUMOR VIRUS.
(E.) Weiss, D. W. (Dept. Immun., Hebrew U.-Hadassah
Med. Sch., Jerusalem, Israel), A. Sulitzeanu, L.
Kung, M. Adelberg and Y. Segev. *Israel J Med Sci*
7(1):187-201, 1971.

Highly inbred BALB/cCrg1 mice, free of mammary tumor
virus were given s.c. immunizing implants of 1 mm³
fragments of living tumor or living normal lactating
mammary tissue derived from an isogenic nursing
female or normal tail skin grafts taken from the
tumor donors, which were surgically removed when
tumors reached an approximate size of 5 x 5 mm or
after a period of 4 wk. Ten days later, sera were
collected by groups; the animals were challenged by
i.c. injection into the left inguinal region of a
freshly prepared suspension of viable tumor cells.
A pronounced increase in the incidence of progressive
tumors as a function of time resulted after challenge
in the tumor-immunized group. Repeat experiments,
using tumor tissue in the 9th transplant generation
compared to the 4th of the initial experiment,
revealed no significant differences in tumor inci-
dence between the differently pretreated groups; 50
to 75% of the mice developed cancers and the growth
rate in the tumor-and lactating mammary gland-
immunized groups was moderately enhanced. Animals
receiving pooled sera 6 hr before challenge with
tumor cells developed tumors somewhat later with a
slightly lowered incidence in the mice given serum
from the tumor bearers. Challenge of animals with

5 other types of tumor cells and heart-kidney frag-
ments (used as controls) revealed generally no
difference in the incidence of tumor development;
however, a time-related enhancement or repression
of tumor growth following challenge was seen after
immunization with pooled sera.

- 2403 BASIC PROTEINS AND SYNTHETIC POLYNUCLEOTIDES
AS MODIFIERS OF IMMUNOGENICITY OF SYNGENEIC
TUMOR CELLS. (E.) Braun, W. (Inst. Microbiol.,
Rutgers U., State U. New Jersey, New Brunswick), O.
J. Pleska, J. Raskova and D. Webb. *Israel J Med
Sci* 7(1):72-82, 1971.

Mice immunized with tumor cell homogenates or whole
tumor cells in conjunction with Freund's adjuvant
and pertussis vaccine were challenged with s.c.
injections of methylcholanthrene-induced sarcomas
or virus-induced ascites tumor cells. The incidence
of recurrence of excised tumors in vaccinated ani-
mals (4-27%) was consistently lower than that ob-
served in nonvaccinated animals (22-48%) for a
period from 7-39 days. The incidence of tumor
takes after challenge with the chemically-induced
tumor cell line revealed that the achievable pro-
tection was specific for the cell line employed for
immunization and did not extend to independently
derived tumor cell lines, including those induced
by the same carcinogen in the same inbred strain of
mice. Growth rate was lower in animals of the
tumor-excised, vaccinated group compared to animals
from the tumor-excised, nonvaccinated group. Treat-
ment with polyadenylic-polyuridylic acid after ex-
cision of syngeneic chemically-induced tumor cells
or at the time of implantation of virus-induced
cells decreased the frequency of recurrence or
rate of tumor growth.

- 2404 PROLIFERATION OF MACROPHAGE AND GRANULOCYTE
PRECURSORS IN RESPONSE TO PRIMARY AND TRANS-
PLANTED TUMORS. (E.) Hibberd, A. D. (Cancer Res. Unit,
Walter and Eliza Hall Inst., Melbourne, Australia) and
D. Metcalf. *Israel J Med Sci* 7(1):202-210, 1971.

The response of "in vitro colony-forming cells" (CFC)
to primary or transplanted syngeneic tumors and the
effect of tumor growth on colony-stimulating factor
(CSF) levels was studied in mice of strains AKR, BALB/c,
C3H, CBA, C57BL, 129/J and the F1 hybrids (NZB x
C57BL)F1 and (BALB/c x C57BL)F1. Almost all of the
AKR mice with spontaneous lymphoid leukemia exhibited
elevated levels of granulocyte and monocyte levels,
probably due to an increased production rather than a
prolonged intravascular life span of these cells.
The femur content of in vitro CFC was highly variable
in the leukemic mice, but 5 of 27 leukemic mice had
elevated levels and 14 of 27 had depressed levels of
in vitro CFC. Serum levels of CSF were elevated in
most leukemic mice, but there was no correlation
between serum CSF and either bone marrow content of
CFC or blood white cell levels. The incidence of in
vitro CFC was consistently elevated in the spleen of
mice bearing a variety of s.c. transplanted syngeneic
tumors at a stage when the tumor mass approximated
10-20% of body wt, compared to control animals; levels

of CSF and blood white cells were uniformly elevated in tumor-bearing animals. A detailed time study of the host response to HPC-28 and WEHI-10 tumors was made in BALB/c and C3H mice. When BALB/c tumor HPC-28 (H-2b) cells were injected into 129/J(H-2d), CBA(H-2k) and B10D2(H-2b) mice, no detectable tumor growth occurred in any of the recipients, although there was a rise in *in vitro* CFC. HPC-28 and WEHI-10 were found to contain low levels of CSF and the contents did not change significantly with progressive enlargement of the tumors.

- 2405 EXPERIMENTAL MODELS FOR EVALUATION OF HOST DEFENSES IN CANCER. (E.) Stern, K. (Dept. Life Sci., Bar Ilan U., Ramat Gan, Israel) and A. Goldfeder. *Israel J Med Sci* 7(1):42-51, 1971.

Immune responses to sheep RBC were determined at 5, 10 and 14 days after immunization in mice of strains X/Gf, IBA, C57BL/S and C3H/S that had been subjected to total body X-irradiation of 300 R 4, 7 and 12 days previously; reticuloendothelial cell phagocytosis of ^{51}Cr -labeled sheep RBC was assayed in tumor-free and tumor-bearing (injected s.c. with syngeneic mammary tumor cells) mice. Significantly lower levels of antibodies (from agglutinin and hemolysin values) were found in all groups of irradiated mice compared to controls regardless of strain and timing of immunization. At the termination of the experiments on day 14, X/Gf mice immunized 4 and 7 days after irradiation exhibited 18-60% greater spleen weights than control animals; the increase was paralleled by the presence of increased lymphoid tissue. In reticuloendothelial cell phagocytosis assays, significant impairment of splenic phagocytosis occurred in all tumor-bearing C3H/S mice but not in X/Gf mice. Splenomegaly was more pronounced in tumor-bearing X/Gf than in C3H/S animals. Hepatomegaly was seen in tumor-bearing mice of both strains, but hepatic phagocytosis was not significantly affected by X-irradiation.

- 2406 RECOGNITION OF LEUKAEMIA CELLS AS FOREIGN BEFORE AND AFTER AUTOIMMUNIZATION. (E.) Powles, R. L. (Chester Beatty Res. Inst., Surrey, England), L. A. Balchin, G. H. Fairley and P. Alexander. *Brit Med J* 1(5747):486-489, 1971.

The reactivity *in vitro* of leukemic lymphocytes against autologous leukemic cells following autoimmunization was investigated. Leukemia cells in the peripheral blood of 9 patients with acute leukemia were collected and stored with dimethylsulfoxide (DMSO) in tissue culture medium 199 at -179°C . Lymphocytes from peripheral blood of the same patients in remission were cultured with the thawed autologous leukemia cells. Autoimmunization was achieved with stored leukemia cells subjected to irradiation (at 4°C at a concentration of 10^8 cells/ml with a dose of 10,000 rads using ^{60}Co γ -irradiation at 1,500 r per min); the cells were injected within 30 min into all 4 limbs both intradermally and s.c. Stimulation of remission lymphocytes by stored autologous leukemia cells occurred in all 9 patients.

Autoimmunization led to increased stimulation of patient lymphocytes within a few days; it also affected their capacity to respond to normal allogeneic cells. Those cases where allogeneic stimulation was below the normal range before autoimmunization showed an increase in their response, and cyte recognition of leukemic cells was more pronounced than recognition of allogeneic cells. The lymphocytes seemed to have responded in both a specific and a non-specific manner following autoimmunization. It was not possible to determine, under the experimental conditions used, whether the antigen(s) in human acute leukemia is individually specific or chemically-induced animal tumors or "group" specific as in the neoantigens of virus-induced tumors, or the cause of interference by transplantation antigens.

- 2407 COEXISTENCE OF INTRASPECIES AND INTERSPECIES SPECIFIC ANTIGENIC DETERMINANTS ON THE MAJOR STRUCTURAL POLYPEPTIDE OF MAMMALIAN C-TYPE VIRUSES. (E.) Gilden, R. V. (Flow Lab. Inc., Rockville, Md.), S. Oroszlan and R. J. Huebner. *Nature* 231(21):107-108, 1971.

Gel diffusion assays using various selected sera against mouse, hamster and cat crude and purified C-type viral antigens indicated that the cross-reactive antigenic determinants were specifically located on the major structural polypeptides of C-type viruses. When analyzed in SDS-acrylamide gel electrophoresis, mouse (MuLV), hamster (HaLV) and cat (FeLV) C-viruses disrupted by SDS, urea and mercaptoethanol were shown to possess 3 distinct major polypeptide components. The slowest migrating of these components (molecular wt 26,000-35,000) clearly carried the major group-specific determinants (gs-1) common to C-type viruses. These group-specific antisera showed a high degree of specificity for their homologous viruses in both complement-fixation and gel diffusion assays. However, sera from a few rats bearing murine sarcoma virus-induced transplant tumors, from rats immunized with homogenates of such tumors (MSV-I-1) reacted strongly with both HaLV and infected cells and purified virus after ether extraction. MSV-I-1 and guinea pig anti-MuLV-gs-1 reacted with both disrupted virus pellets and purified MuLV to give lines of identity; MSV-I-1 4 times gave 2 bands with the slow moving peptide component. Partial identity reactions were observed between the slow moving component and MuLV, HaLV and FeLV, suggesting that both species specific determinants and interspecific determinants reside on the same molecule. Absorption tests, heat inactivation kinetics and cross reactivity tests confirmed these results.

- 2408 RESISTANCE AND SUSCEPTIBILITY TO TRANSFERRING VI. REACTION OF LABELLED LYMPHOID CELLS TRANSFERRED INTO THE SITE OF PREVIOUSLY IMPLANTED CARCINOMA. (E.) Dvorak, R. (Dept. Path., U. Hamburg, Germany) and J. Lindner. *Neoplasma* 18(1):63-86, 1971.

Strain BALB/c and CBA/j mice were pretreated with Endoxan prior to receiving transplanted Bo4 cells.

oma or Ehrlich ascites carcinoma cells in the upper lip; 5 hr after tumor transplantation, mice were given injections of ^3H -thymidine-labeled lymphoid cells from syngeneic animals. Isolated lymphoid cells were from the lymph nodes, spleen or thymus of donor mice; in some cases the lymphoid cell donors had been immunized with living tumor cells. Following injection of the labeled lymphoid cells to the region of the tumor transplant, the lymphoid cells disintegrated; thymic cells disintegrated more quickly after injection than did splenic cells or lymph node cells. Of lymphoid cells found in the tumor region, lymphocytes and "differentiated blast cells" were markedly more abundant than fibroblasts, polynuclear leukocytes, or other mesenchymal cells. Preimmunization of lymphoid cell donors accelerated the rate of disintegration of injected spleen and lymphoid cells in the tumor-bearing hosts. In all mice implanted with the Bo4 carcinoma, some round-nucleated lymphocytes and spleen cells transformed themselves into fibroblasts and other mesenchymal cells composing the periblastomatous connective tissue and tumor mass.

DETECTION OF ANTIGENIC SUBUNITS OF A MURINE LEUKEMIA VIRUS BY PASSIVE HEMAGGLUTINATION-INHIBITION. (E.) Sibal, L. R. (Nat'l. Cancer Inst., Nat'l. Inst. Hlth., Bethesda, Md.), V. W. Anderson, Jr. and M. A. Fink. *J Immunol* 106(4):1050-1055, 1971.

Passive hemagglutination test modifications which identify clearly the viral antigen-antibody reactions for study and methods of separation of such viral antigens are presented. The purified Rauscher leukemia virus (RLV) used to sensitize tanned sheep erythrocytes was the 1.16 g/ml isolate of supernatant fluid from infected tissue cultures. Antiserum to RLV was prepared in Rhesus monkeys and BALB/c mice by standard methods. Tween 80-ether treatment of purified RLV released 2 antigenic subunits which could be separated into highly purified subunits by density gradient centrifugation and column chromatography. One of these was identified as a group-specific antigen as seen from the reaction between tanned sheep erythrocytes coated with ether-treated virus and mouse antiserum. The other was identified to be an envelope antigen of the virion; its inhibition of the reaction between tanned sheep erythrocytes coated with tween-ether- or deoxycholate-treated virus and mouse antiserum free of anti-group-specific antigen indicated it to be a group-specific antigen of the virus. Antiserum to RLV produced in monkeys agglutinated tanned sheep erythrocytes coated with both antigens, while BALB/c antiserum reacted only with the envelope antigen. The usefulness of the passive hemagglutination-inhibition reaction for the independent assay for each of these antigens is emphasized.

IMMUNOLOGICAL STUDIES ON MOUSE MAMMARY TUMORS AND LEUKEMIA. (E.) Dmochowski, L. (Texas M.D. Anderson Hosp. Tumor Inst., Houston),

W. C. Williams, G. R. Swearingen, B. Myers and S. Fujinaga. *Texas Rep Biol Med* 29(1):41-62, 1971.

Intravenous inoculation of New Zealand white rabbits with mouse mammary tumor virus (MTV) from milk of RIII/Dm and of A/Dm high-mammary-cancer strain mice produced immune sera that appeared to be specific for the whole MTV virion. One of the precipitate lines produced by the anti-MTV sera against MTV antigens from milk of these 2 strains contained characteristic type B (or MTV) particles. This precipitate line was not removable by absorption with tissue preparations from low-mammary-cancer strain mice; its appearance was found to be prevented upon testing of the immune sera against milk of mice with low incidence of mammary cancer (BALB/C/Dm or C57BL/6/Dm). Immunodiffusion tests revealed a similarity of the MTV from different strains of mice. The anti-MTV serum gave a positive mixed hemadsorption reaction (MHA) with both spontaneous and induced mouse mammary tumors containing MTV (type B particles) and/or MLV (type C particles). A negative MHA reaction occurred with a cell line derived from an induced mammary tumor in a BALB/c/Dm strain mouse where no type B or type C virus particles could be found by electron microscopy. Positive MHA reactions with the anti-MTV serum were obtained with cultures of leukemic tissues, of mouse embryos and of a 3-methylcholanthrene-induced mouse sarcoma, all shown to contain type C particles. The MHA reaction of the investigated anti-MTV serum appeared to be specific for both MTV and MLV. Positive MHA reactions were given also by an anti-MLV serum with cultures of leukemic tissues, mouse mammary tumors and mouse embryo tissues containing type C particles; this reaction appeared to be due to the presence of antibodies to heterophile and viral antigens in MLV infected tissues. The positive MHA reaction given by anti-MTV and anti-MLV sera with tissues containing both type B and type C particles indicates the presence of antibodies to type C particles in the investigated anti-MTV sera and the widespread presence of MLV.

2411 AN APPROACH TO THE IMMUNOLOGICAL REGRESSION OF THE TUMOR. (E.) Kobayashi, H. (Hokkaido U. School of Med., Sapporo, Japan). *Acta Path Jap* 20(4):441-450, 1970.

Immunological features of Friend virus-induced tumors in Wistar King Aptekman/Mk rats are reviewed. Inoculation of Friend virus in newborn rats produces leukemia or lymphosarcoma within 5-7 months; these neoplasms are referred to as rat Friend tumors (RFT). RFT do not grow well in adult isologous strain rats, their growth occurs only in Friend virus-tolerant or immunologically immature rats, in which the primary target organs appear to be the spleen and the thymus. Cytotoxic tests and electric charge studies showed that the growth patterns of the RFT tumors are closely related to the cell membrane surface properties. The chromosome pattern of the RFT appears to present fewer anomalies than other neoplasms. The poor transplantability characteristics in isologous rats seem to be due to a membrane antigen originating from the Friend virus.

which is associated with the transplantation antigen, referred to as virus-specific transplantation antigen (VSTA). Reference is made to certain neoplastic cell cultures which under certain conditions of *in vitro* cultivation (i.e., exposure to 4-nitroquinoline-N-oxide) lose their oncogenicity upon inoculation into experimental animals; this phenomenon is referred to as disdifferentiation and may be due to a mutation of the tumor cell. (16 references)

- 2412 HOST RESPONSE IN SPONTANEOUS REGRESSION OF MURINE LEUKEMIA. (E.) Rich, M. A. (Albert Einstein Med. Ctr., Philadelphia, Pa.) and R. Clymer. *Cancer Res* 31(6):803-807, 1971.

Serum from strain Swiss ICR/Ha mice that had been inoculated with a strain of Friend leukemia virus, which gives rise to spontaneously regressing leukemia, was injected into mice; in the donor mice leukemia had appeared and regressed following inoculation of the virus. The capacity of sera to confer immunity to Friend leukemia virus was tested. Leukemia developed in 1 of 9 infected mice given serum from mice bearing regressed leukemias, while in infected mice given serum from normal mice and from leukemic mice, leukemia developed in 8 of 9 and 9 of 10 mice, resp. Infection and leukemia development did not induce resistance to reinfection with Friend leukemia virus. Whereas mice inoculated with the strain of Friend virus which gave rise to regressing tumors showed a high incidence of leukemia regression, mice inoculated with both the regressing strain of virus and with a strain of Friend virus which produced persistent leukemia developed leukemia which did not regress.

- 2413 FELINE LEUKAEMIA VIRAL ANTIGENS AND ANTISERA TO THE GROUP SPECIFIC ANTIGENS OF THE MURINE LEUKAEMIA VIRUSES. (E.) Sarma, P. S. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), R. J. Huebner, H. C. Turner, R. V. Gilden and T.-S. Log. *Nature* 230(10):50-52, 1971.

The interspecies immunological reaction between the murine and feline C-type viruses has been applied to the quantitative study of the feline leukemia viruses (FuLV). Murine sarcoma virus (MSV) rat serum pools were prepared by mixing Fischer rat sera carrying transplanted syngeneic sarcomas induced by the Moloney strain of MSV. Pool 20 was prepared from sera which gave complement fixation antibody titers greater than 1:80 against Murine leukemia virus (MuLV) tissue culture viral antigens and MSV rat tumor antigens. The broad reacting pool 21 was prepared in the same manner, except that it included several rat sera which also reacted with antigen preparations of murine tissues containing the C-type viral genome that had no infectious features such as non-producer MSV rat tumors. The feline leukemia and sarcoma group specific antiserum used in complement fixation assays of feline C-type viruses was prepared in a beagle by the induction of a fibrosarcoma with the GA strain of feline sarcoma virus (GA-FSV). The tissue culture complement

fixation antigen induction test for FeLV and FSV was performed by inoculation of the virus into feline embryo fibroblast (FEF) monolayer culture and by determination of the subsequent occurrence of the viral group specific antigens in these cultures. MSV rat serum pools 20 and 21 reacted in complement fixation tests with feline virus specimens such as purified virus preparations, clarified 20% extracts of feline lymphosarcoma and cell culture antigens of FEF infected with the FeLV and FSV. Titres obtained with MSV pool 20 were lower than those revealed by MSV rat serum pool 21, which were identical to those given by the feline group specific antiserum prepared in a beagle. The group of the noncytopathogenic FeLV in FEF cultures was readily detected by complement fixation tests with the broad reacting MSV pool 21. The usefulness and sensitivity of the broad reacting MSV pool 21 for detection of FeLV is emphasized after comparison with results obtained by other techniques.

- 2414 STUDIES ON THE LOCALIZATION OF RADIOLABELLED ANTIBODIES TO A MOUSE MYELOMA PROTEIN. (E.) Reif, A. E. (Dept. Surgery, Tufts Med. Sch., Boston, Mass.). *Cancer* 27(6):1433-1439, 1971.

Cell suspensions of plasma cell tumor fragments incubated with ^{125}I -antibody and normal ^{131}I - γ -globulin for 30 min were injected s.c. into young adult BALB/c female mice. All mice injected with 50,000 or more cells died with tumors and those injected with 5,000 or fewer cells survived permanently without evidence of tumor growth at any time. In tumor cells incubated with paired-labeled antibody, the addition of increased amounts of the mixture resulted in the binding of an increased proportion of antibody. *In vivo* results of paired-labeled antibody injections revealed that injection of unlabeled whole antiserum to protein M 3 hr prior to the paired-labeled mixture appeared to reduce the proportion of antibody relative to normal γ -globulin that remained present in blood, muscle, kidney and tumor tissue. Radiolabeled antibody injections revealed the rate of excretion to be estimated at 42% per day, while that of normal γ -globulin was only 24% per day. Localization of antibody in tumor was obtained only in 1 group of mice in which the localization index relative to kidney was 13.1, 5.9 and 6.8, resp., and relative to muscle was 5.7, 1.86, and 2.0 resp., giving an average of 8.6 fold increase in localization of antibody in tumor over kidney and a 3.2 increase over muscle.

- 2415 ANTIBODY AGAINST NEOPLASTIC PLASMA CELLS. I. SPECIFIC SURFACE ANTIGENS ON MOUSE MYELOMA CELLS. (E.) Watanabe, T. (Roswell Park Memorial Inst., Buffalo, N. Y.), Y. Yagi and D. Pressman. *J Immunol* 106(5):1213-1221, 1971.

Surface antigens were found on strain BALB/c mouse myelomas which were not present on lymphocytes, liver and kidney cells. Rabbit antisera were raised against cellular components of mouse myelomas and

against lymph node cells. Cells of 6 myeloma lines were used in immunization and fluorochromasia cytotoxicity tests. Sera cytotoxic to all the myeloma lines were obtained which were not cytotoxic to normal lymph node cells. Absorption with myeloma sediments readily removed the myeloma-cytotoxic antibodies from the sera; however, sediments from thymus liver and kidney failed to remove the myeloma-cytotoxic antibodies. Antisera which were cytotoxic to 1 of the myeloma lines were cytotoxic to the other lines; no antigens specific to any 1 line were detected. While lymphocyte-cytotoxic antisera were developed which yielded lymphocyte-cytotoxic antibodies when treated with lymph node, spleen or thymus sediments, sediments of myeloma cells and of liver and kidney cells were not effective in removing antibodies from lymphocyte-cytotoxic sera.

16 EVOLUTION OF CELL-MEDIATED IMMUNITY IN MICE BEARING TUMORS PRODUCED BY A MAMMARY CARCINOMA CELL LINE. INFLUENCE OF TUMOR GROWTH, SURGICAL REMOVAL, AND TREATMENT WITH IRRADIATED TUMOR CELLS. (E.) Le Francois, D. (Gustave-Roussy Inst.), K. Youn, J. Belehradsky, Jr. and G. Barski. *J Nat Cancer Inst* 46(5):981-986, 1971.

Bred adult female mice of the mammary tumor virus-free C3HeB/Fe strain were inoculated s.c. with a cell line (TMI) from a spontaneous mammary tumor of C3H mouse, and peritoneal cells obtained from washings of the peritoneal cavity following tumor formation were used to test TMI colony growth inhibition *in vitro*. Inhibition approximated 64-100%; the peritoneal cells demonstrated specificity by their inability to suppress colony growth of other, unrelated homologous tumor cells. Between the 7th and 9th day after inoculation of the initial tumor cells in 3 experiments, the peritoneal cell inhibition was 21% and in all cases, 16 days or later when the tumor size was 7 mm or more in diameter, peritoneal cells entirely lost their inhibitory capacity; peritoneal cells from animals bearing huge tumors seemed to have an enhancing effect on cell growth. Surgical removal of the tumors 35-40 days after inoculation of TMI resulted in a return of specific cell immunity in peritoneal cells spontaneously and reached high levels by the 23rd day after surgery. Peritoneal cells from animals receiving trypsinized irradiated tumor cells from the excised tumor on the 1st postoperative day showed a 59% inhibitory activity on day 10 compared to 24% activity in cells from the control group and lack of reactivity in cells from a group of animals receiving homologous spleen cells following surgical removal of the tumor. The role of lymphocytes and macrophages in inhibiting target cell colony growth *in vitro* is unclear.

17 NATURAL ANTIBODIES IN NORMAL HUMAN SERA AGAINST THE EHRlich MOUSE ASCITES TUMOUR IDENTIFIED WITH THE AID OF COMPLEMENT COMPONENTS, UTILIZING CLASSICAL REAGENTS. (E.) Oravec, C. Cancer Res. Inst., Slovak Academy of Sciences,

Bratislava, Czechoslovakia) and J. Cambelova. *Neoplasma* 18(2):141-159, 1971.

Undiluted and/or diluted (up to 1:8) sera from 93 samples of venous blood from 20 clinically healthy donors were incubated with Ehrlich mouse ascites tumor cells; these samples and the same sera without tumor cells (controls) were examined for complement levels before and after absorption with tumor cells. Values before absorption in undiluted samples ranged from 75.75-157.44 U/ml and after absorption from 0.70-94.512 U/ml, a decrease of 17%-99%. Dilutions of sera in a 1:2 and 1:4 ratio resulted in a diminution of complement in absorbed fractions which were statistically significant, but dilutions after the original sera had been freed from complement by absorption did not show any diminution in values. The cytotoxic activity of natural antibodies in normal human sera against the tumor cells was not markedly affected by application of heat at 56°C for 20 min and in one instance was stimulated when cells were suspended in a veronal buffer. However, complement levels and viable cell titrations did not show any correlation.

2418 TUMOR-DISTINCTIVE CELLULAR IMMUNITY TO HUMAN SARCOMA AND CARCINOMA. (E.) Vanky, F. (Karolinska Inst., Stockholm, Sweden) and J. Stjernswärd. *Israel J Med Sci* 7(1):211-220, 1971.

Lymphocytes obtained from the peripheral venous blood of 20 cancer patients preoperatively were mixed with autochthonous tumor tissue cells in which DNA synthesis had been blocked by mitomycin-C and incubated at 37°C for 5 days followed by the addition of ³H-thymidine for 12 hr. The lymphocytes were stimulated to increased DNA synthesis by the autochthonous tumor cells in 11 patients with an index above 1.5. The lymphocytes from these 11 patients were stimulated by allogeneic cells with a reactivity index of 2.5-10.3. DNA synthesis in allogeneic effector lymphocytes from a healthy donor was stimulated to a greater extent (>2-fold) by the lymphocytes than by tumor cells taken from the same patient. Autochthonous lymphocytes were stimulated more frequently (7 of 12) by the tumor cells than were the allogeneic lymphocytes (4 of 12). Sarcoma cells stimulated allogeneic lymphocytes less frequently than did carcinoma cells. These *in vitro* tumor-distinctive cellular immune reactions were also observed between autochthonous frozen and thawed tumor cells and lymphocytes and between lymph node cells draining the tumor and autochthonous lymphocytes.

2419 SERUM CONCENTRATIONS OF γ G, γ A AND γ M IMMUNOGLOBULINS IN PATIENTS WITH CARCINOMA, MELANOMA, AND SARCOMA. (E.) Hughes, N. R. (Prince of Wales Hosp., Randwick, Australia). *J Nat Cancer Inst* 46(5):1015-1027, 1971.

Sera from 256 normal controls and 984 patients with carcinoma of nonhematopoietic tissue were analyzed for concentrations of γ G, γ A and γ M immunoglobulins by means of ammonium sulfate fractionation and

chromatographic techniques. Male patients with carcinoma of the skin or ulcerative colitis and male and female patients with lung cancer had mean γG concentrations significantly increased above normal. Male controls as well as male patients with all cancers had significantly higher γA concentrations; significantly higher mean concentrations of γA were observed among male patients with carcinoma of the skin, colon and rectum ($0.01 > P > 0.001$), and lung ($0.02 > P > 0.01$). For females, higher than normal γA concentrations were found in patients with carcinoma of the mouth, colon, rectum, and uterus. Female controls had a significantly higher mean γM concentration than male controls ($0.001 > P$). Female patients with melanoma had a significantly higher mean γM concentration than male patients with melanoma ($0.001 > P$). Male patients with sarcoma and female patients with melanoma had a mean γM concentration significantly higher than normal, while patients with primary cancer of the ovary had a γM mean concentration significantly lower than normal. Normal males had a significantly higher mean $\gamma A/\gamma G$ ratio than normal females ($0.001 > P$). A significantly higher mean ratio of $\gamma A/\gamma G$ in males than in females was also found for patients with cancers of the lung ($0.01 > P > 0.001$), mouth ($0.05 > P > 0.02$), colon and rectum ($0.001 > P$), and cancers of the mouth and gut combined ($0.001 > P$); in males the mean $\gamma A/\gamma G$ ratio was significantly increased above that of normal controls in patients with cancer of the mouth, stomach, duodenum, colon and rectum. For females, this ratio was significantly increased above controls in patients with cancer of the mouth, colon and rectum, and uterus.

- 2420 ANTIGENICITY OF TWO ESTABLISHED TUMORIGENIC CELL LINES ESTIMATED BY THE MIGRATION INHIBITION TEST. (E.) Kieler, J. (Fibiger Lab., Kgs. Lyngby, Copenhagen, Denmark) and K. Ostrowski. *Proc Soc Exp Biol Med* 137(1):130-134, 1971.

Inbred strains of C₃H and DBA/2 mice were immunized by s.c. injection of two sarcoma tumor cell lines (L-1 and L-2c) and reimmunized after 1-6 wk; the immunological response was challenged *in vivo* by the s.c. transplantation of 0.2 ml of minced C₃H-L1 and C₃H-L2c tumor tissue and *in vitro* by the migration inhibition test. The low incidence of mice with progressively growing tumors following preimmunization (0-18%) with L-1 and L-2c cells and challenge with *in vivo* propagated C₃H-L1 tumor indicated that common isoimmunizing antigens were present in the 2 cultured cell lines and the C₃H-L1 tumor. An absence of similar protection against the C₃H-L2c tumor suggested that this tumor did not share these antigens. However, cross-reaction between the cultured L-2c cells and the C₃H-L2c tumor was demonstrated by the migration inhibition test *in vitro*; the negative result of the transplantation test in immunized mice was interpreted as a manifestation of the high virulence of the C₃H-L2c tumor.

- 2421 INDUCTION OF LONG TERM LYMPHOCYTE LINES FROM DELAYED HYPERSENSITIVE HUMAN DONORS USING SPECIFIC ANTIGEN PLUS EPSTEIN-BARR VIRUS. (E.)

Baumal, R. (Albert Einstein Coll. Med., Bronx, N. Y.) B. Bloom and M. D. Scharff. *Nature* 230(9):20-21, 1971.

Peripheral white cells from delayed hypersensitive subjects were used to establish selective antigen sensitive cells in culture by combined exposure to specific antigen and Epstein-Barr virus (EBV) *in vitro*. Venous blood was collected from healthy donors with delayed skin reactions either to tuberculin (PPD 0.0001 mg) or to streptokinase-streptodornase (SKSD 10 U). Aliquots of white cell suspension containing 8×10^6 cells/ml in culture medium were incubated in the presence or absence of 5 μ g of PPD or 50 μ g/ml of SKSD. The cells were then treated with EBV (incubation at 37°C for 1 hr). Controls included cells which received antigen but not EBV, cells which received EBV but no antigen and cells which received neither EBV nor antigen. Cell growth was observed 6 wk after initiation of the cultures. Continuous lines were established only from cells treated with the combination of EBV and antigen to which the donor was sensitive (according to the skin reactivity to PPD or SKSD). These cultures continued to produce a variety of fully or partially assembled immunoglobulin molecules constituting 5-30% of the newly synthesized cytoplasmic proteins. No evidence was found whether these cells were antigen sensitive or whether they were producing specific antibodies. Untreated or antigen alone-treated cells failed to grow. When treated with virus alone, cells showed transient growth with no further propagation.

- 2422 AN INHERITED MURINE SERUM COMPONENT RELATED TO MAMMARY CANCER. (E.) Berrington, P. (Bio-Res. Inst., Cambridge, Mass.), R. E. Berrington and C. H. Yoon. *Proc Soc Exp Biol Med* 137(1):5-1971.

A murine serum trace component (SMT-antigen) was found to be a genetically determined characteristic transmissible by either sex. Reciprocal crosses made between C₃H/HeJ mice (of which 90% of the females are positive for SMT-antigen) and BALB/c mice (of which none of the virgin females show positive SMT-antigen reactions). F₁ mice were crossed to F₁ littermates and backcrossed to either parent strain. Although only females exhibit the serum antigen, both reciprocal crosses produced serum positive females with nearly equal frequencies. Every type of backcross to BALB/cJ parents produced certain proportions of SMT-antigen-positive females. Involvement of an infectious factor was ruled out by breeding BALB/cJ females first with C₃H/HeJ males, then BALB/cJ males; no SMT-antigen was found in offspring of the latter mating. Foster-nursing experiments eliminated the possibility of milk transmission of an infectious agent. The distribution of SMT-antigen-positive and -negative F₂ hybrids and backcross offspring indicated the presence of a pair of modifier genes, which prevent the expression of major SMT-antigen genes when present in a recessive homozygous condition. This SMT-antigen component may represent the genetic factor involved in the formation of spontaneous mammary tumors in mice.

3 ANOMALOUS ANTIGENS IN EXPERIMENTAL HEPATOCARCINOGENESIS. (Rus.) Khundanova, L. L. N. Petrov Res. Inst. Oncol. U.S.S.R. Ministry of Health, Leningrad). *Vop Onkol* 17(3):85-90, 1971.

une sera against liver or hepatoma antigens of s receiving 10 mg dimethylaminoazobenzene (DAB) ly p.o. for 300 days were obtained 4, 15, 30, 60, and 400 days after the beginning of carcinogen inistration. Double gel diffusion, immunoelectro-esis and complement fixation reactions indicated t 4 specific anomalous antigens were formed during hepatocarcinogenic process. Immunoelectrophoretic ility showed that anomalous antigen I occurring ly at 4-30 days was within the α -globulin zone; gen II detected in the albumin and α -globulin e and antigen III in the β - and γ -globulin zone rred within 30, 60 and 100 days of the process. gen IV which was isolated from hepatomas and h migrated to the albumin and α -globulin region detected at 400 days of hepatocarcinogenesis. of the 4 anomalous antigens (I and IV) were d to be organ specific for liver cells and it assumed that all 4 types of antigens participate the DAB-induced hepatocarcinogenesis.

EVIDENCE FOR IMMUNOLOGICAL SURVEILLANCE DURING SKIN CARCINOGENESIS: INFLAMMATORY IN IMMUNOLOGICALLY COMPETENT MICE. (E.) Lappe, Cancer Res. Genet. Lab., U. California, Berkeley). *Israel J Med Sci* 7(1):52-65, 1971.

microscopic features of skin tumor formation and ination were studied in isografts of 3-methyl-anthrene-treated skin transplanted to female /cCrgl mice with varying degrees of immunologic etence; the latter was achieved by pretreatment BCG(MER) or saline injections, sublethal whole-X-irradiation (450 R), or antilymphocyte serum) injections. Three to 4 grafts were examined each group 9-39 days after grafting. Micro-ic papillomas were commonly seen in sections n from grafts transplanted 2-4 wk after grafting. he 3rd wk after grafting, papillomas were rved in about 20% of the hosts which had received er X-irradiation or ALS treatment, but macroscopic llomas were not seen in immunologically competent s till after the 4th wk postgrafting. Focal s of intense lymphocytic infiltration were found ng the latent period of papilloma development in etent but not in depressed hosts. The presence lymphocyte exocytosis in conjunction with dermal tin debris from former epithelial pearls were d in MER-stimulated hosts 25-39 days after graft- these sites may represent the residue of for-microscopic papillomas. The total number of oscopic and macroscopic papillomas recorded in etent hosts was 25 out of a total of 62 grafts ared to 34 papillomas in the 56 grafts made to essed hosts. When inflammatory foci are included the tabulation of papilloma group totals, there actually comparable numbers of lesions in the etent and depressed groups. This observation is istent with the possibility that in competent s a portion of the incipient papillomas were

destroyed at a microscopic level and were later scored as inflammatory foci, as predicted by the theory of immunological surveillance.

2425 EFFECT OF IMMUNE STATUS ON THE DEVELOPMENT OF ARTIFICIALLY INDUCED METASTASES IN DIFFERENT ANATOMICAL LOCATIONS. (E.) Vaage, J. (U. Texas M.D. Anderson Hosp. Tumor Inst. Houston), K. Chen and S. Merrick. *Cancer Res* 31(5):496-500, 1971.

Twelve-wk-old male mice of an inbred strain C3Hf/Bu were challenged with fibrosarcoma cells 1 day after destruction by irradiation or surgical removal of 18-day-old sensitizing fibrosarcoma implants. Controls without presensitizing implants and animals given sublethal whole-body irradiation 1 day before challenge were also challenged with fibrosarcoma cells. The mice that had been cured of their sensitizing tumor implants had acquired a high degree of resistance to challenge; booster injections of killed tumor cells on days 7 and 14 after challenge enhanced the resistance and only 0-33% of the animals developed tumors compared to a 5-52% tumor incidence in presensitized animals without booster, a 50-95% tumor incidence in controls and a 75-100% tumor incidence among those receiving irradiation.

2426 TUMOR-SPECIFIC ANTIGENS IN 2-ACETYLAMINO-FLUORENE-INDUCED RAT HEPATOMAS AND RELATED TUMORS. (E.) Baldwin, R. W. (British Empire Cancer Campaign Res. Labs., U. Nottingham, England) and M. J. Embleton. *Israel J Med Sci* 7(1):144-153, 1971.

Wistar rats of both sexes treated with 0.04% dietary 2-acetylaminofluorene (AAF) or 0.006% diethylnitrosamine (DENA) developed hepatocellular carcinomas, ear duct squamous cell carcinomas and nephroblastomas. AAF- and DENA-induced tumor cell preparations were used to immunize other rats against subsequent tumor cell challenge; in some cases, immunizing tumor cells were exposed to ^{60}Co γ -irradiation prior to injection into rats. Tumor-specific transplantation antigens were detected in 3 of the 9 AAF-induced hepatomas by the capacity of irradiated (15,000 r) immunizing grafts to induce resistance against challenge. AAF-induced hepatomas were only weakly immunogenic; immunized rats only rejected challenges with low numbers of tumor cells. Immunizing inocula which conferred immunity against a challenge with 10^4 tumor cells failed to immunize against 2×10^4 tumor cells. The low immunogenicity of AAF-induced liver tumors was further demonstrated by their inability to induce reproducible tumor-specific humoral antibody reactions detectable by membrane immunofluorescence tests. Resistance to challenge inocula of $1-2 \times 10^5$ cells of the immunizing tumor was seen following immunization with DENA-induced hepatomas. Resistance to challenge with ear-duct carcinomas induced by AAF was seen in all but 1 mouse challenged with 5×10^4 ear-duct carcinoma cells; however, this resistance broke down a subsequent challenge with 10^5 tumor cells. No resistance was seen against nephroblastomas.

- 2427 THE INFLUENCE OF CARCINOGENIC NITROSAMINES ON THE INDUCTION OF SERINE DEHYDRATASE IN THE RAT LIVER. (Ger.) Jennissen, H. (Biochem. Inst., U. Freiburg, Germany), J. Hoshino and H. Kröger. *Z Krebsforsch* 75(4):246-252, 1971.

Sprague-Dawley rats were given N-nitrosomorpholine (10 mg/kg) or diethylnitrosamine (4 mg/kg) in drinking water daily, and the effects of these agents on the induction of serine dehydratase by casein hydrolysate and by fasting were observed. Neither carcinogen affected the induction of serine dehydratase by casein; however, the induction of the enzyme by fasting was potentiated by diethylnitrosamine. N-nitrosomorpholine did not affect fasting induction of serine dehydratase. An increase in enzyme synthesis was thought to be the cause of the increased activity induced by fasting.

- 2428 TRANSFER OF IMMUNITY TO TUMOUR ISOGRAFTS BY THE SYSTEMIC ADMINISTRATION OF XENOGENIC "IMMUNE" RNA. (E.) Deckers, P. J. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and Y. H. Filch. *Nature* 231(23):181-183, 1971.

Guinea pigs were given injections of cells from a benzopyrene-induced rat sarcoma containing tumor-specific transplantation antigens and after 9-11 days RNA was extracted from spleens and lymph nodes. This guinea pig RNA was used to immunize rats which were challenged with cells from a benzopyrene-induced sarcoma. RNA from immunized guinea pigs produced a resistance to challenge which exceeded the resistance manifested by unimmunized rats and by rats immunized with "nonspecific" RNA. By day 28 after challenge, only 5 of 20 rats given RNA from immunized guinea pigs had developed sarcomas, whereas 12 of 21 rats given "nonspecific" RNA and 17 of 21 unimmunized rats had developed sarcomas. In other experiments, RNA prepared from guinea pigs inoculated with benzopyrene-induced sarcomas containing tumor-specific transplantation antigen was used to immunize strain C₃H/HeN mice against sarcoma cell challenge. RNA from immunized guinea pigs protected mice against tumor development.

- 2429 ENHANCEMENT OF TUMOUR HOMOGRAFTS BY THE LOCAL GRAFT-VERSUS-HOST REACTION. (E.) Medzihradsky, J. (Cancer Res. Inst., Slovak Academy of Sciences, Bratislava, Czechoslovakia), M. Klobusicka, E. Konikova and L. Novotna. *Neoplasma* 18(2):133-140, 1971.

F₁ hybrid (Lw×BD) rats were challenged with MC-1 ascitic tumor cells and parental BD spleen cells by s.c. inoculation into the right flank; other F₁ hybrid (Lw×AVN) rats were given tritium-labeled spleen cell grafts by footpad injection. In animals challenged with both tumor and spleen cells, progressive tumor growth was observed in all animals compared to controls, which were given either mixtures of tumor with syngeneic spleen cells or tumor injections without spleen cells and in which regression occurred between 15-25

days following challenge. On the 6th day of the footpad-induced reaction (with parental spleen cells), ³H-thymidine injection resulted in the labeling of the small lymphocytes in the spleen; the label was steadily depleted until the 12th day when no label was found. Allogeneic spleen footpad injections showed 5% of small lymphocytes remaining labeled on day 12.

- 2430 INCREASED INCIDENCE OF SPONTANEOUS LUNG ADENOMAS IN MICE FOLLOWING NEONATAL THYMECTOMY. (E.) Trainin, N. (Dept. Exp. Biol., Weizmann Inst. Sci., Rehovot, Israel) and M. Linker-Israeli. *Israel J Med Sci* 7(1):36-41, 1971.

Inbred SWR/Jax mice were thymectomized at 3 days of age and the incidence of spontaneous lung adenomas arising in these animals was observed. Forty-percent of the thymectomized mice and 14% of the non-thymectomized mice developed tumors in 7 months. At the age of 13 months, tumor incidence in thymectomized and nonthymectomized animals was 44% and 14% resp. Thymectomized Swiss strain mice also developed lung tumors more frequently than nonthymectomized mice of the same strain. The number of peripheral blood lymphocytes was not significantly reduced after thymectomy in either SWR or Swiss mice; however, the immune response to sheep red blood cells was lower in thymectomized animals than in intact controls. In SWR mice, titers of hemolysins and hemagglutinins were decreased following thymectomy. Also impaired by thymectomy was the homograft response to tumor cell transplants; transplantation of a solid fibrosarcoma to intact and thymectomized mice resulted in 0% and 86% tumor takes, respectively.

- 2431 EFFECTS OF HETEROLOGOUS ANTILYMPHOCYTE ANTIBODY ON THE DEVELOPMENT OF SPONTANEOUS AND TRANSPLANTED LYMPHOMA IN AKR MICE. (E.) K. P. (Baylor Coll. Med., Houston, Tex.), K. S. and J. J. Trentin. *Cancer* 27(5):1161-1166, 1971.

Male pathogen-free AKR strain mice were given rabbit serum or rabbit anti-mouse thymocyte serum s.c. injections of 0.1 ml every third day and death the presence of absence of spontaneous lymphoma was noted. Untreated mice developed lymphoma at a rate of 52 wk of age; lymphoma incidence in mice given normal rabbit serum was similar to that in untreated mice. In mice given anti-lymphocyte serum (ALS), mortality from lymphoma was accelerated with 100% of mice dying with lymphoma by 48 wk of age. In a repeat experiment, accelerated spleen enlargement, probably leukemic, occurred; however, the time elapsed from commencement of treatment to death from leukemia did not differ appreciably between ALS-treated mice and in untreated controls. In a related experiment, ALS-treated mice were challenged with cells from a syngeneic thymoma. ALS treatment delayed death from thymoma in treated mice.

- 2432 RELEASE OF A NON-SPECIFIC CYTOTOXIC FACTOR BY SPLENIC CELLS IMMUNIZED AGAINST ALLOGENEIC TUMOUR CELLS. (E.) Hottier, D.

N.S.E.R.M., Vandoeuvre-les-Nancy, France), M. ner and C. Burg. *Rev Europ Etud Clin Biol* 3):240-243, 1971.

een cells from unimmunized Swiss B strain mice, from mice immunized against allogeneic tumor ls, were placed in one compartment of a 2-part mber. Tumor target cells prepared from a enzopyrene-induced rhabdomyosarcoma in Swiss B e were placed in the other compartment. unized mice received injections of a methylcho-threne-induced rhabdomyosarcoma of strain C₃H e. Both compartments were inserted beneath the n of a Swiss B strain mouse and allowed to remain place for 5-8 days; on removal from the mouse, or target cells in their compartment were counted. n tumor target cells were implanted in mice mpanied by spleen cells from an unimmunized se without added tumor cells or by spleen cells m an unimmunized mouse with allogeneic tumor cells, number of target cells recovered from their com- tment ranged from 1.39×10^6 cells/ml to $4.45 \times$ cells/ml. However, when tumor target cells e implanted in mice together with spleen cells m mice immunized against allogeneic tumor cells ytotoxic effect was seen to be operating on the or cells. Cell counts recovered from the tumor l compartment ranged from 0.23×10^6 cells/ml to 6×10^6 cells/ml.

3 RESISTANCE AND SUSCEPTIBILITY TO TUMOURS: V. ON THE PERMEATION OF THE ³H-THYMIDINE ELLED CELLS FROM LYMPHATIC ORGANS INTO THE SITE PROLIFERATING TUMOUR. (E.) Dvorak, R. (Dept. h., U. Hamburg, Germany) and J. Lindner. *plasma* 18(1):41-62, 1971.

e of strains BALB/c and CBA/j and Wistar strain s were given implantations of either Ehrlich ites carcinoma cells or Bo4 carcinoma cells intra- ally, or i.p.; tumor-bearing animals were given . injections of ³H-labeled lymphoid cells from een, lymph nodes, or thymus of syngeneic animals ch had been given repeated administrations of tri- ted thymidine. Labeled lymphoid cells were found monly in the lymph nodes and spleen, and more ely in the thymus, lung and liver, of tumor- ring animals. While no labeled lymphoid cells e found in the vicinity of the proliferating or transplants in rats, some labeled cells pene- ted to the upper lip of mice (the site of the nsplanted Bo4 carcinoma). In some cases, the ors of lymphoid cells had been immunized with ing tumor cells. In tumor-bearing rats given phoid cells from immunized donors the labeled phoid cells disintegrated more rapidly than el cells from unimmunized donors. In mice en lymphoid cells from immunized donors, there a slight increase in the number of labeled phoid cells in the region of the transplanted or. Some labeled fibroblasts were found in the nity of the Bo4 carcinoma; these fibroblasts e apparently transformed mononuclear lymphoid ls from the ³H-labeled inocula.

2434 INFLUENCE OF HOST FACTORS ON LEUKEMOGENESIS BY THE RADIATION LEUKEMIA VIRUS. (E.)

Haran-Ghera, N. (Dept. Exp. Biol., Weizmann Inst. Sci., Rehovot, Israel). *Israel J Med Sci* 7(1):17-25, 1971.

The leukemogenic activity of a cell-free centrifugate (CFC), prepared from a radiation leukemia virus-induced lymphoma was assayed by administration of the virus preparation into male C57BL/6 mice of varying immunological competence; virus was injected 1) i.p. into mice aged 24 hr or less, 2) into an 8-day-old isogenic thymus grafted under the kidney of thymec- tomized young adult hosts, a group of which were exposed to 400 R whole-body irradiation 3 days later or 3) into one lobe of the intact thymus of young adult animals, a group of which was exposed to 400 R whole-body irradiation 3 days later. The leukemo- genic agent induced 55% lymphoid tumors at an average latent period of 175 days in newborn mice, compared to 90% or 97% incidence and a latency of 84-95 days in irradiated mice which had received vi- rus injection into a thymus graft or into intact thy- mus; the incidence of lymphoid leukemia among mice in thymus inoculated groups that were not irradiated was 15-25%. Whole-body irradiation with buffer injection resulted in an 8% lymphoid leukemia inci- dence with an average latent period of 200 days. Virus-inoculated mice were also subjected to thymic irradiation, antithymocyte serum (ATS), normal rabbit serum (NRS) or urethan treatment. Local irradiation of thymus did not enhance tumor development, but ATS and urethan treatment increased leukemia induction 50% and 53%, resp., compared to virus inoculation alone; NRS had a slight co-leukemogenic effect. Delaying host treatment after inoculation of the leukemogenic virus into the thymus reduced the leu- kemia incidence in the different groups, although no decrease in virus viability in the thymus was found over a period of several wk; this decrease in leukemia development was attributed to an immuniza- tion phenomenon.

2435 PHYTOHEMAGGLUTININ UNRESPONSIVENESS IN MOUSE SPLEEN CELLS INDUCED BY METHYL- CHOLANTHRENE SARCOMAS. (E.) Adler, W. H. (Dept. Path., U. Florida Coll. Med., Gainesville) T.

Takiguchi and R. T. Smith. *Cancer Res* 31(6): 864-867, 1971.

The cellular composition of spleen cells from methylcholanthrene-induced tumor-bearing and tumor- free A/J and CBA mice was investigated using dis- continuous albumin density gradients. Normal spleen cells were predominantly dense, small lymph- ocytes while spleen cells from sarcoma-bearing mice were predominantly larger and less dense. The response to phytohemagglutinin (PHA) of spleen cells from tumor-bearing and tumor-free mice was observed; ³H-thymidine incorporation by cells from tumor-bear- ing animals was less responsive to PHA than were cells from tumor-free animals. Cells from tumor- bearing mice stimulated with PHA incorporated 41,326-63,951 cpm ³H-thymidine/culture while normals

incorporated 151,023 cpm/culture; spleen cells from tumor-bearing mice from which the tumors had been excised incorporated 143,846 cpm/culture. In another experiment, mice were immunized with sheep red blood cells (SRBC) and the response of their spleen cells to PHA was compared to that of unimmunized mice. Normal CBA mouse spleen cells stimulated with PHA incorporated 180,013 cpm ^3H -thymidine/culture, while spleen cells of mice immunized with 1 or 3 injections of SRBC incorporated 113,889 or 71,274 cpm/culture, resp. A shift in spleen cell cultures of immunized mice toward less dense cell types was also seen.

2436 RESISTANCE TO ROUS SARCOMA ELICITED BY IMMUNIZATION WITH LIVE VIRUS. (E.)

Sigel, M. M. (Dept. Microbiol., U. Miami Sch. Med., Fla.), P. Meyers and H. T. Holden. *Proc Soc Exp Biol Med* 137(1):142-146, 1971.

Chickens were immunized with subtumorigenic doses of Rous sarcoma virus (Rous-associated virus) once every 2 wk for 6 wk using a 10^{-8} dilution of virus; 3 wk after the last immunizing injection, birds were challenged with 100 tumorigenic doses of the Rous-associated sarcoma virus. While 100% of unimmunized chickens developed sarcoma, only 6% of immunized birds developed sarcoma. When immunization of chicks was effected with a 10^{-9} dilution of virus only 4% of birds developed tumors as a result of the immunizing virus injections compared to 25% of birds immunized with a 10^{-8} virus dilution. However, the 10^{-9} immunizing virus dose afforded only slight protection from tumor development to chickens challenged with virus following immunization. When chicks were immunized with a Rous-associated leukosis virus and challenged with Rous-associated sarcoma virus, 27% of birds immunized with 2 injections of Rous-associated leukosis virus and 9% of birds given 3 immunizing injections of virus developed sarcomas compared to 100% of unimmunized chickens. Neutralization tests on sera of immunized and unimmunized birds showed that 68 and 100%, resp., of sera from birds given 2 and 3 injections contained antiviral antibody; none of the sera from unimmunized birds contained antiviral antibody.

2437 EVIDENCE FOR COMMON ANTIGENIC SITES BETWEEN THE SURFACE OF SHEEP ERYTHROCYTES AND THAT OF CERTAIN VIRUS-TRANSFORMED HAMSTER CELLS. (Fr.)

Meyer, G. (Res. Dept. C.R.A.C.M., Marseille, France), C. de V. Saint Cyr and M.-A. Nosny. *C R Acad Sci* 272(14):1928-1931, 1971.

The membrane antigens of SV-40- or polyoma virus-transformed BHK cells appeared to be common to the surface antigens carried by sheep or guinea pig erythrocytes. Absorption methods revealed the antigens elicited by SV-40 transformation to have a constitution similar to that of the Forssman antigen, while the glycoproteins of the polyoma virus-transformed cells and the sheep erythrocyte appeared to differ from the Forssman antigen. Immunofluorescence showed the surface antigens of

hamster tumor cells (CT 54 strain) and the surface antigens of BHK 21/13 polyoma virus-infected cells to be specific to the viral infection and transformation. No such antigens were found on normal BHK 21/13 cells. The virus specific sites on the surface of the transformed cells were associated with an unmasking of a number of glycoprotein groups of which N-acetylgalactosamine and N-acetylglucosamine were the most frequent haptens. These molecules occurred on the surface of fresh or boiled sheep erythrocytes and on the surface of guinea pig erythrocytes and were common constituents of the Forssman type antigen. These data confirmed those found by O'Neil and Black.

2438 EVIDENCE FOR TUMOR-SPECIFIC IMMUNITY IN HUMAN MALIGNANT MELANOMA. (E.) Nag

G. A. (Dept. Internal Med., Bürgerspital, Switzerland), W. F. Piessens, M. M. Stilmant and F. Lejeune. *Europ J Cancer* 7(1):41-47, 1971.

Tumor cells and lymphocytes were collected from a 68-yr-old male patient with cutaneous malignant melanoma metastasizing to the regional lymph nodes. Lymphocytes taken from the patient on the day of resection of the tumor and at various times thereafter were reacted with tumor cells. Blastoid transformation of lymphocytes did not occur with lymphocytes taken on the day of the operation or reacted with tumor cells. However, lymphocytes taken on day 41 postoperation were stimulated by tumor cells; the stimulation was suppressed by autologous serum taken and stored on the day of operation. It was thought that lymphocyte transformation was an indicator of cell bound tumor specific immunity, and that immunity became manifest only after the removal of the primary tumor. Immunosuppressive serum taken on the day of operation was thought to have contained antibodies which blocked the lymphocyte stimulation.

2439 SERUM ALLOTYPE LOSS DUE TO A LYMPHOID TUMOR IN CHICKENS. (E.) David, C.

(Dept. Human Genetics, U. Michigan, Ann Arbor), O. J. Fletcher. *J Immunol* 106(6):1673-1676, 1971.

Loss of certain serum antigens upon tumor development was investigated in White Leghorn chickens. Thirty 6- to 10-wk-old chickens were inoculated with 0.5 ml of minced transplantable lymphoid material (TLT) in the pectoral muscle. Tumors developed within 4-5 days following inoculation. Three controls were used: 1) birds injected with normal lymphoid tissue; 2) birds injected with transplantable lymphoid tumor inactivated by freezing and thawing; and 3) birds without any treatment. Blood samples were taken by cardiac puncture and 7-13 days after tumor inoculation. The pre- and post-inoculation sera were tested for the typical antigens at the 3 genetic loci *a*, *b* and *c*. In 12 cases in which the pre-TLT serum was positive, the post-TLT serum failed to form a precipitin line. The 6 controls and 18 test birds gave clear precipitin lines for the 2 serum series.

allotype loss occurred most frequently with antigens C2 and C3. The *b* locus antigen disappeared only 3 cases; in the other cases either the *a* or *c* locus antigen disappeared. In 2 cases a positive reaction appeared in the post-TLT sera when it was negative in the pre-TLT sera. Except for the C2 and C3 antigens only one antigen at each locus disappeared. To check this observation, chickens were mated so as to obtain birds heterozygous at the 3 loci and injected similarly to TLT injection. The controls showed identical patterns for the pre- and post-TLT sera. In most cases only one of the antigens appeared to be inactivated. Allotype *a*1 was inactivated more often (5/9) in this experiment than in the first. The tumor mince came from a different group of birds for the second experiment. IgG was slightly depleted in the post-TLT sera when tested against rabbit antichickens whole serum. A band found close to the antigen well in the pre-TLT sera and suspected of being IgA was absent in the post-TLT sera. The allotype loss seemed to be due to a specific interaction with the growing tumor either by binding to neoplastic cells, thereby enhancing tumor growth, or by virus infiltration of specific stem cells, preventing further differentiation.

TUMOR IMMUNITY: TUMOR SUPPRESSION IN VIVO INITIATED BY SOLUBLE PRODUCTS OF SPECIFICALLY STIMULATED LYMPHOCYTES. (E.) Bernstein, D. (Div. Biol. Stand., Natl. Inst. Hlth., Bethesda, Md.), D. E. Thor, B. Zbar and H. J. Rapp. *Science* (1984):729-731, 1971.

Matched, adult, Sewall-Wright NIH inbred strain-2 guinea pigs were injected intradermally with 0.1 ml of ascites cells of transplanted diethylnitrosamine-induced hepatomas following immunization with migration inhibiting factor. On day 14, the intradermal tumor nodule measured 15 mm² and 9.3 mm² in control animals compared to lack of growth in immunized animals. At a site adjacent to the migration inhibiting factor-mediated rejection of tumor cells, the size of tumor papules on day 14 was 16.2-19.9 mm² in both immunized and control animals, indicating that a systemic adjuvant effect was not involved. Inhibition of growth of tumor cells implanted at sites of skin incisions 24 hr following immunization indicated that tumor rejection was due to the immune response of lymphocytes rather than to a direct effect by migration inhibiting factor.

TUMOR-ASSOCIATED IMMUNOGLOBULINS. (E.) Witz, I. P. (Dept. Microbiol., Tel Aviv Univ., Israel.). *Israel J Med Sci* 7(1):230-238, 1971.

Moloney lymphoma ascites cells removed from strain 2 mice 9-11 days after implantation were added to a mixture containing ¹³¹I-labeled globulin from rabbit anti-mouse globulin antiserum and ¹²⁵I-labeled normal rabbit globulin and incubated for 60 min at 37°C. Increasing numbers of Moloney lymphoma cells absorb increasing proportions of anti-immunoglobulin antibodies; label uptake was inhibited by the addition of excess unlabeled globulin isolated from the

same rabbit anti-mouse globulin antiserum. Tissue of primary benzo(a)pyrene-induced sarcomas contained at least 10 times more immunoglobulin (IgG) than normal tissue. A higher immunoglobulin IgG₂ fraction was eluted from fast growing tumors and from primary, rather than secondary, tumors. Tumor-associated immunoglobulins IgG₂ may represent specific antibodies directed against determinants of tumor cells.

2442 ANTILYMPHOCYTE SERUM AND ENHANCEMENT. (E.) Takasugi, M. (Dept. Med. Microbiol., U. California, Los Angeles) and W. H. Hildemann. *Israel J Med Sci* 7(1):221-229, 1971.

Antiserum produced in rabbits against Sarcoma I, an A strain tumor (Sa I), or anti-A/Sn spleen cell antiserum was injected into groups of A.BY mice previously inoculated with Sa I tumor cells. Three of 5 mice given anti-Sa I antiserum and 5 mice given anti-A/Sn spleen cell antiserum showed prolonged tumor survival time. Lymphocytosis accompanied the rejection of the tumor in untreated control mice, whereas treated mice challenged with Sa I showed a slight decrease in lymphocyte count on the day following treatment with recovery by day 4. Mice treated with antiserum and without tumor challenge exhibited a marked lymphopenia of several days. The present results confirmed that cytotoxic action against lymphocytes is a major cause of the decline in peripheral lymphocyte levels after anti-lymphocyte serum treatment.

2443 CARBOXY-TERMINAL STRUCTURE OF THE α CHAIN OF HUMAN IgA MYELOMA PROTEINS. (E.) Prahl, J. W. (California Inst. Tech., Pasadena), C. A. Abel and H. M. Grey. *Biochemistry* 10(10):1808-1812, 1971.

The α chains of several human IgA myeloma proteins were subjected to cyanogen bromide cleavage and the carboxy-terminal octapeptides of the proteins were isolated. The Edman degradation and sequence of the carboxy-terminal peptide was: (Met)-Ala-Glu-Val-Asp-Gly-Thr-Cys-Tyr. Proteins of the IgA₁ and IgA₂ protein subclasses showed the same sequence. The ultimate tyrosine residue was present in less than stoichiometric amounts, perhaps as a result of carboxypeptidic activity *in vivo*. It was found in the cleavage experiments using cyanogen bromide that the penultimate half-cystine must be present as an asymmetric inter-heavy-chain bond in order for it to be involved in disulfide bonding of polymeric forms.

2444 HAPTEN BINDING STUDIES ON MOUSE IgA MYELOMA PROTEINS WITH ANTIBODY ACTIVITY. (E.) Sher, A. (Salk Inst. Biol. Studies, San Diego, Calif.) and H. Tarikas. *J Immunol* 106(5):1227-1233, 1971.

The mouse IgA myeloma proteins S23, S63, S107, S129 and J539, having antibody specificities for either phosphorylcholine, ϵ -DNP-caproic acid or galactoside derivatives, were characterized in terms of affinity

for their respective haptens. The immunoglobulins were found to be homogeneous in their affinity for hapten and they showed association constants between 2×10^3 and 1.1×10^6 l/mole on equilibrium dialysis measurements. Binding activity was associated with the Fab fraction of each of the proteins. Unfractionated S107 protein in serum and the reduced and alkylated monomer purified by immunoadsorption had 2 sites/156,000 U molecular weight. Trypsin digestion of the S107 protein showed a Fab fraction in 64% yield with 1 site/53,000 molecular weight. Fractional numbers of binding sites were obtained using chromatography, gel filtration and repeated dialysis to purify the protein.

2445 HYPOLIPIDEMIA DURING MYELOMA. (Fr.)

Fiessinger, J.-N. (Lab. Clin. Chem., Paris, France), M.-P. Ollier, S. Filitti-Wurmser and L. Hartmann. *Ann Biol Clin* 29(1):25-37, 1971.

The serum lipid alterations occurring in 17 patients with IgA and 40 patients with IgG myeloma were reflected in lower levels of total lipids (decreased from 7 g/l in normal subjects to 4.8 g/l in IgA and to 6.3 g/l in IgG myeloma patients), of phospholipids (from 2.4 to 1.5 and 1.9 g/l, resp.), and of total cholesterol levels (from 2.2 to 1.3 and 1.8 g/l, resp.); no variations in the triglyceride levels were observed. α -Lipoprotein levels were decreased in 15 of 15 cases and the β -lipoproteins decreased in 9 of 15 IgA myeloma patients. Serum levels of α -lipoproteins were decreased in 25 of 36 patients with IgG myeloma, and β -lipoproteins were normal in 26 of 36 of these patients. Hypolipidemia was related to hypolipoproteinemia and appeared to be severe in IgA and minor in IgG myeloma patients. The average pathological globulin level was 38.4 g/l (ranging from 8-75 g/l) in sera from IgA myeloma patients and were associated with a decrease in albumin levels (from 43 to 34 g/l). The average pathological globulin level was 43.6 g/l (reaching 100 g/l in one case) in the IgG myeloma patients and seemed to vary according to its sudanophilic or non-sudanophilic properties. IgG elicited no sudanophilic properties; the sudanophilic properties were possibly due to variations in the γ_1 , γ_2 , γ_3 or γ_4 subgroup of the heavy chain constituents of the myeloma IgG. Analytical ultracentrifugation revealed at least 1 additional peak in 11 of 13 IgA myeloma sera and 6 sedimentation peaks in 5 of these sera as compared to the 3 S_1 , S_2 and S_3 sedimentation peaks occurring in normal sera; no supplementary sedimentation peaks were observed in the sera of 13 IgG myeloma patients. Correlation studies showed that hypolipoproteinemia involved mainly the α -lipoproteins. The protein alterations were not related to the type of the pathological immunoglobulin, and the decrease in lipids was more manifest with the increase in myeloma globulin, particularly in case of IgA myeloma.

2446 CELLULAR IMMUNITY INDUCED BY ROUS SARCOMA VIRUS IN JAPANESE QUAIL: I. EFFECT OF ANTILYMPHOCYTE SERUM ON ONCOGENESIS OF ROUS SARCOMA

VIRUS. (E.) Yamanouchi, K. (Dept. Measles Virus Natl. Inst. Hlth., Musashi-Murayama, Tokyo, Japan) and M. Hayami. *Jap J Med Sci Biol* 23(6):395-402, 1970.

Japanese quail spleen cells were inoculated into rabbits 3-4 times weekly; rabbits were bled at the end of the course of inoculations and the antilymphocyte serum (ALS) thus obtained was injected in amounts of 0.2 ml daily for 4 wk into Japanese quails. ALS-treated quails were subsequently infected in the wingweb with Schmidt-Ruppin strain sarcoma virus (100 ID₅₀). Tumors developing in quails not treated with ALS regressed in all cases, whereas only 2 of 9 tumors developing in quails treated with ALS regressed. All of 5 quails treated with normal rabbit serum instead of ALS and 6 of 6 untreated quails were resistant to a tumor-inducing dose of virus, while only 1 of 7 ALS-treated birds was resistant. Tumor metastases were found in liver, spleen and proventriculus of 3 of 7 ALS-treated birds, and in none of the control birds. 8 wk after virus challenge, 70% of quails in all experimental groups had developed virus-neutralizing antibodies.

2447 ANTIGENIC RELATIONSHIPS BETWEEN CELL MEMBRANES OF NORMAL AND SV40 TRANSFORMED RENAL KIDNEY CELLS. (E.) Kedar, E. (Dept. Immunology, Hebrew U.-Hadassah Med. Sch., Jerusalem, Israel), M. Wiener, N. Goldblum and S. Sulitzeanu. *Israel J Med Sci* 7(1):132-142, 1971.

The antigenic relationships of cell lines derived from baby hamster kidney, hamster kidney cells transformed *in vitro* by SV40 and SV40-induced tumors were studied by means of rabbit antiserum against these tissue and sheep RBC. The antisera to the normal kidney cell membranes showed fluorescent antibody staining reactions of only 5-10% at all concentrations tested and the staining of tubular membranes were most pronounced; antisera to the tumor cell membranes stained the kidney glomeruli, the solid tumor cells and both cell lines intensely. Three antigens were distinguished: F antigen was present in all cell types, antigen in the glomeruli, and KT antigen was found mainly in the normal kidney tubules. Solid tumor cells bore less radioactivity than hamster kidney cells; specificity for binding was shown by the high degree of radioactivity bound to hamster kidney cells and leukemic cells in response to labeled antibodies specific to these cells.

2448 IMMUNOLOGIC RESPONSE OF MICE BEARING LEUKEMIA L1210. (E.) Bonmassar, E. (Microbiol. Assoc., Inc., Bethesda, Md.), A. Bonmassar, S. Vadlamudi and A. Goldin. *Cancer Res* 27(6):1356-1362, 1971.

The number of direct plaque-forming cells (PFC) in spleen was determined in normal and in leukemic mice at several stages of leukemic growth with or without therapy or following chemotherapy with an alkylating agent.

gent 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU). Mouse strains used included the oncogenic-resistant 7BL/10ScSn and the hybrid CDF₁ (DBA/c DBA/2 Cr male x BALB/c female). Mice were given injections of leukemic cells followed after 2, 3, 4 or 5 days of injections of antigenic sheep red blood cells (SRBC). When SRBC were injected 2 or 3 days after leukemic transplantation, PFC/spleen counts were normal or somewhat elevated ($10^{5.5}$ PFC/spleen). When SRBC were administered 4 or 5 days after the transplantation of leukemic cells, PFC/spleen counts were depressed (10^5 PFC/spleen). The antibody response seemed to be reduced only in mice subjected to antigenic stimulation after a certain stage of leukemic growth. In a related experiment, mice were immunized with SRBC following transplantation of fast- and slow-growing leukemic cells. Immunosuppression was seen only in mice given fast-growing leukemic cells in which SRBC was injected 5 days before the median day of death for mice; in contrast, immunosuppression was not seen in mice with slow-growing leukemia given SRBC 7 days before the median death day. Leukemia remission induced by BCNU did not prevent the immunosuppression of leukemic mice, although the same treatment schedule did not interfere with antibody production in non-leukemic animals.

49 VARIATION IN IMMUNOSENSITIVITY OF SV40-TRANSFORMED HAMSTER CELLS. (E.)

Veithia, S. S. (Baylor Coll. Med., Houston, Tex.), L. McMillan, P. M. Kaplan and S. C. Bushong. *Immun* 106(5):1295-1300, 1971.

Four-week-old hamsters were immunized by s.c. injections of 10^6 PFU of SV40 given once a wk for 3 wk and then challenged with cells from one of 2 cell lines derived from a hamster tumor originally infected by SV40; both these cell lines contained SV40 and T antigens. Of the 2 cell lines used to challenge the hamsters, one was immunosensitive (H-50 IS) and one was immunoresistant (H-50 IR). SV40-immunized hamsters rejected the challenge with H-50 IS cells; however, H-50 IR cells produced tumors in challenged hamsters. H-50 IR cells contained SV40-specific transplantation antigens; they rendered hamsters immune to challenge with H-50 IS cells. Both sensitive and resistant hamster tumor cells grew at the same rate *in vitro*, and both were inhibited to an equal degree by SV40 immune serum.

50 IMMUNOGLOBULIN, PROTEIN AND NUCLEIC ACID SYNTHESIS IN CULTURED MYELOMA CELLS. (E.)

Emmel, Ch. B. (Dept. Biol., U. Oregon, Eugene). *Cell Res* 65(1):202-208, 1971.

Cultured mouse myeloma cells were studied to determine the point at which the synthesis of immunoglobulin-coding messenger RNA molecules was most sensitive. Cultures in which overall cell growth had stopped showed the highest level of immunoglobulin synthesis relative to total protein synthesis; in these cultures, immunoglobulin synthesis amounted

to 30% of total protein synthesis. In cells where growth had ceased, however, total protein synthesis was low and since the production, content, and transport of RNA was constant at all times, it was concluded that the turnover of RNA in the nongrowing cells was high. Addition of fresh medium to the culture markedly increased cell turnover. While total protein synthesis in the late exponential stage of cell growth was similar to the exponential stage, the rate of immunoglobulin synthesis amounted to 10-20% and was on the increase. It was thought that the synthesis of immunoglobulin coding mRNA molecules was maximal at the late exponential phase of cell growth.

2451 POLYCLONAL IMMUNOGLOBULIN DEFICIENCY IN MYELOMATOSIS AND MACROGLOBULINAEMIA. (E.)

Cwynarski, M. T. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.) and S. Cohen. *Clin Exp Immun* 8(2):237-248, 1971.

Immunoglobulin (Ig) levels were compared in 118 patients with monoclonal protein disease (MPD) and it was found that polyclonal Ig was significantly reduced in 82% of the patients. Ig deficiency was equally frequent with all classes of monoclonal Ig, but was considerably more common in patients with myelomatosis than in patients with benign MPD. Normal values for electrophoretic heterogeneity and for proportions of κ - and λ -chains were found in polyclonal IgG taken from sera containing monoclonal IgG, IgA or IgM. In lymph nodes of patients with macroglobulinemia, monoclonal protein was synthesized; but monoclonal proteins were not synthesized by nodes from myelomatosis patients. Apparently spread of cancerous cells accounts for polyclonal Ig deficiency in macroglobulinemia but not in myelomatosis.

2452 INHIBITION OF MIGRATION OF HUMAN AUTOGENOUS AND ALLOGENEIC LEUKOCYTES BY EXTRACTS OF PATIENTS' CANCERS. (E.)

Wolberg, W. H. (Div. Clin. Oncol., U. Wisconsin Med. Ctr., Madison). *Cancer Res* 31(6):798-802, 1971.

Leukocytes and lymphocytes from peripheral blood were incorporated into Pasteur pipets with solution derived from normal or carcinomatous human tissue and studied for migration. Inhibition of leukocyte migration was found in 15 of 21 tumors tested and exceeded the migration seen with normal preparations in only 3 instances. Tissue preparations from a foreign body granuloma caused a 30% inhibition, whereas migration was unaffected by benign adenomatous polyps. Ultrasonic disruption of tumors produced preparations that effectively inhibited migration, and phytohemagglutinin produced inhibition of both leukocyte and lymphocyte migration dependent upon the concentration present in the migrating medium. 6-Mercaptopurine was effective in reversing the effect of phytohemagglutinin but not that of tumor preparations.

- 2453 THE INDUCTION OF PRECIPITATING ANTIBODIES TO THE MAMMARY TUMOR VIRUS IN SEVERAL INBRED MOUSE STRAINS. (E.) Hilgers, J. (Netherlands Cancer Inst., Amsterdam), J. H. Daams and P. Bentvelzen. *Israel J Med Sci* 7(1):154-160, 1971.

Mice of strains C57BL, 020, BALB/c, GR, C3Hf, Ceh, RIIIf, and RIII were injected i.p. with approximately 5 µg purified Bittner mammary tumor virus (MTV-S) preparation in Freund's adjuvant or with purified virus disrupted with ether; blood samples were taken 1-3 weeks after booster treatment of 20 µg of virus every 2-3 months. Antibodies to complete mammary tumor virus particles were detected in sera from immunized mice of every strain studied. Sera taken 21 days after the first booster with complete particles revealed that C3H and BALB/c gave no reaction at all. Most of the other sera reacted only with the P antigen (the virion and the assumed intact nucleoid). The RIII sera gave the strongest reactions with the P antigen, and, except for one 020 serum, they were the only sera which reacted with the membrane-soluble antigen of the disrupted virus. Sera taken after the 2nd booster showed strongest reactions when obtained at 14 days; a positive reaction was observed in each mouse strain to the complete virions at this time. After the 3rd and 4th booster, each mouse strain gave many positive reactions; C3H and BALB/c mice showed positive reactions with complete virions also. In female mice immunized with ether-treated virus and not given boosters, most sera reacted with nucleoid soluble antigen; GR and C57Bl strains failed to react with membrane soluble antigen.

- 2454 STUDIES ON CELLULAR AND HUMORAL IMMUNITY TO TUMOR-SPECIFIC ANTIGENS IN POLYOMA VIRUS-INDUCED TUMORS OF RATS. (E.) Datta, S. K. (Rega Inst. Med. Res., U. Leuven, Belgium) and M. Vandeputte. *Cancer Res* 31(6):882-889, 1971.

Inhibition of colony formation in cultures of polyoma sarcoma cells was studied with lymph node and spleen cells from R and BN inbred rats with polyoma virus-induced sarcomas. Lymph node and spleen cells that were sensitized specifically against polyoma tumor antigen and from animals infected with polyoma virus strongly inhibited colony formation by polyoma kidney sarcoma cells when compared with controls. Cells from 7 of 8 animals with primary tumor significantly reduced the colony number, and cells from all of 4 rats inoculated with virus as newborns showed a significant reduction in colony number. All of the 5 sera tested from primary tumor-bearing rats could block most of the inhibitory effect of lymph node and spleen cells from immunized rats or from rats with or without primary tumors, whereas all of the 5 sera from rats with no primary tumor had little or no effect; the blocking effect was specific since it was removable by absorption with polyoma tumor but not with a 7,12-dimethylbenz(a)anthracene-induced tumor. Sera from animals inoculated with the virus as newborns contained cytotoxic antibodies which reduced colony numbers when compared with normal serum.

- 2455 TUMOR-SPECIFIC IMMUNITY IN THE COURSE OF PRIMARY POLYOMA AND ROUS TUMOR DEVELOPMENT IN INTACT AND IMMUNOSUPPRESSED RATS. (E.) Sjöberg, H. O. (Dept. Immun., Fred Hutchinson Cancer Ctr., Pacific Northwest Res. Found., Seattle, Wash.) and K. Borum. *Cancer Res* 31(6):890-900, 1971.

A polyoma tumor and Rous sarcoma resulting from infection of inbred W/Fu and BN rats that were either untreated, inoculated with antilymphocytic serum after infection, thymectomized or sham-operated were utilized for the study of colony inhibitory effects on tumor target cells of rats with or without primary tumors. Significantly higher frequencies of primary tumors were obtained in immunosuppressed animals; although the frequency of primary Rous sarcoma was 100% in both immunologically intact and immunosuppressed rats, a somewhat reduced latency period was seen in the latter. Cell-mediated immunity tests to the tumor-specific transplant antigens of polyoma and Rous sarcomas revealed that lymph node cells of the rat carrying a primary polyoma sarcoma did not inhibit the polyoma target tumor cells, but they significantly inhibited the Rous sarcoma target cells. Sera from 3 of 7 rats carrying primary polyoma tumors has a significant inhibitory effect on the polyoma target tumor cells but did not inhibit Rous sarcoma cells, showing the inhibitory effect is specific.

- 2456 COMPLEMENT FIXATION IN CONVENTIONAL AND REGRESSING VIRUS-INDUCED MURINE LEUKEMIA. (E.) Rich, M.A. (Albert Einstein Med. Ctr., Philadelphia, Pa.), S. Karl and R. Clymer. *J Immunol* 106(6):1488-1492, 1971.

The complement fixation (CF) antibody response of Swiss mice following infection with the regressor Friend virus (RFV) strain was compared to that elicited by conventional strains of murine leukemia virus. Random-bred ICR/Ha Swiss male mice, 4-5 weeks old, were inoculated i.p. with 0.5 ml containing 200 ED₅₀ doses of cell-free virus stocks prepared from 20% suspensions of spleens from leukemic mice previously inoculated with conventional or regressor FV. Sera were obtained 50 days later from mice leukemic by 18 days after inoculation. "regressed" sera were taken from mice leukemic by day 18 and non-leukemic by day 50. Immunization with a conventional strain of murine FV led to an appreciable humoral CF response. RFV-infection led to the appearance of CF antibody in mice in which leukemia had regressed and was absent in leukemic mice. This CF antibody cross-reacted with other strains of murine leukemia virus.

- 2457 THE GROUP-SPECIFIC ANTIGEN AND OTHER TUMORAL PROTEINS OF HAMSTER AND MOUSE CARCINOGENESIS ABSTRACTS 1971. (E.) Oroszlan, S. (Flow Lab. Inc., Rockville, Md.), C. Foreman, G. Kelloff and R. V. Gilden. *Virology* 43(3):665-674, 1971.

Monolayers of hamster embryo cells chronically infected with hamster specific helper virus and rat tumor

carrying the AKR leukemia virus were incubated in medium containing ^3H -uridine and ^3H -amino acids and studied for the presence of group-specific antigen and other structural proteins. Cultures were analyzed by sucrose gradient centrifugation, and clear visualization of ^3H -amino acid label was found at buoyant density of approximately 1.15 g/cm^3 . The protein content of pooled peak fractions totalled $10 \mu\text{g}$, based on absorbance values, with a specific activity of 1.3 complement fixation U/ μg protein of mouse antiserum. Animals immunized with 0.75 of the pH 6.9 fraction provided antisera which were specific for hamster C-type viruses in complement fixation and gel diffusion tests and which were non-reactive with uninfected hamster cells, ether-disrupted murine C-type viruses and its group specific antigen. Studies employing polyacrylamide gel electrophoresis of amino acid-labeled hamster and mouse C-type viruses disrupted by SDS, urea and mercaptoethanol revealed 3 major polypeptides for each virus; their molecular weights were 14,000, 17,500 and 30,000 for hamster virus and 14,000, 23,000 and 35,000 for the mouse virus.

8 RETENTION OF ANTIGEN SPECIFICITY OF MURINE SARCOMA VIRUSES GROWN IN HAMSTER CELLS *IN VITRO*. (E.) Kelloff, G. (Nat'l. Cancer Inst., Div. 1. Inst. Hlth., Bethesda, Md.), R. J. Huebner, H. Chang, S. Oroszlan and R. V. Gilden. *Nature* (5):155-157, 1971.

Neutralization tests were carried out by the focus reduction procedure using 3 sarcoma viruses (a hamster-specific sarcoma virus, M-MSV(HaLV)G; a Rauscher leukodermatoma virus, M-MSV(RLV)/HEF; and a Moloney sarcoma virus, M-MSV(RLV)G grown exclusively on mouse cells) and antisera (anti-M-MSV(HaLV)G from tumor-bearing hamsters and anti-RLV from hamsters immunized with Rauscher leukemia virus-hamster tumors). M-MSV(RLV), whether grown in hamster cell or not, was neutralized by anti-M-MSV(HaLV)G and was not neutralized by anti-M-MSV(RLV)G; M-MSV(HaLV)G was neutralized by its homologous antiserum but not by anti-RLV. Interference tests showed that the helper virus, HaLV, interfered with M-MSV(HaLV)G but not with M-MSV(RLV)/HEF, indicating that the latter does not share envelope antigens with the hamster-specific viruses. The interference mediated by HaLV seems to be specific for hamster viruses and a non-interferon mediated interference. Immunodiffusion and complement-fixation tests showed that M-MSV(RLV)/HEF maintained group-specific antigen after growth in hamster cells and showed no reactivity with antisera against the hamster group-specific antigen. *In vitro* passage of murine sarcoma virus in hamster cells does not seem to cause the complete hamster-specific host range and antigenic change seen after *in vivo* passage in the hamster.

9 THE ADOPTIVE TRANSFER OF CONCOMITANT IMMUNITY TO MURINE TUMOR ISOGRAFTS WITH TUMOR CELLS FROM TUMOR-BEARING ANIMALS. (E.) Kiers, P. J. (Surg. Brnch., Nat'l. Cancer Inst., Bethesda, Md.), B. W. Edgerton, B. S. Thomas and Y. H. Pilch. *Cancer Res* 31(6):734-742, 1971.

Mice of the C57Bl/6 strain were given immunizing or control treatments as follows: 1125 mice were given s.c. inoculations of 10^5 viable cells of a methylcholanthrene-induced sarcoma in the right hind leg; of the 1125 animals given tumor cells, groups of 25 were challenged with injections of 5×10^3 sarcoma cells in the left hind leg 1-28 days after the initial tumor inoculation; some tumor-bearing mice were killed and used as donors of spleen cells which were injected i.p. into previously untreated mice; mice given spleen cells were challenged with tumors 1-21 days after spleen cell inoculation. In mice given an immunizing inoculation of sarcoma cells the challenge inocula took in 0-8% of animals challenged on day 7-28 after tumor cell transfer. The tumor incidence in controls which received no immunizing tumor inoculation was 87-100%. Mice given spleen cells from tumor-bearing mice showed delay in tumor development and reduced tumor incidence compared to mice given spleen cells from tumor-free mice and compared to mice given tumor cell inoculations only.

2460 EFFECT OF SYNGENEIC AND ALLOGENEIC PLASMA ON LYMPHOCYTES FROM CANCER PATIENTS, PATIENTS WITH NON-NEOPLASTIC DISEASES, AND NORMAL SUBJECTS. (E.) Al-Sarraf, M. (Div. Oncol., Wayne State U., Detroit, Mich.), S. Sardesai and V. K. Vaitkevicius. *Cancer* 27(6):1426-1432, 1971.

Blood lymphocytes from cancer patients were cultured with syngeneic plasma or allogeneic plasma (from non-cancer patients or from healthy subjects); lymphocytes were stimulated with phytohemagglutinin, and the blast transformation and mitotic response of the cancer patients' lymphocytes were observed in culture with syngeneic and allogeneic plasma. Blast transformation and mitotic response of cancer patients' lymphocytes were inhibited by allogeneic plasma of either non-cancer patients or healthy subjects. Transformation of lymphocyte from non-cancer patients was also inhibited when plasma from cancer patients or from healthy subjects was added to them in culture. Plasma from cancer patients and from non-cancer patients also inhibited the transformation response of lymphocytes from healthy subjects.

2461 LEUKOCYTE CANDIDACIDAL ACTIVITY AND RESISTANCE TO SYSTEMIC CANDIDIASIS IN PATIENTS WITH CANCER. (E.) Lehrer, R. I. (Cancer Res. Inst., U. California Med. Sch. San Francisco) and M. J. Cline. *Cancer* 27(5):1211-1217, 1971.

Leukocytes collected from patients with metastatic solid tumors, lymphoma, Hodgkin's disease (stages I-IV) and multiple myeloma were incubated with the pathogen *Candida albicans*. The ability of the leukocytes to ingest and/or kill the pathogen was observed. While neutrophils from patients with neoplastic disease were able to ingest *Candida*, cells from patients with advanced Hodgkin's disease and with acute leukemia showed impaired ability to kill *Candida*. Patients with metastatic tumors on chemotherapeutic regimens also showed impaired candidacidal capacity. Some of the neutrophils which

showed diminished candidacidal activity also showed low levels of myeloperoxidase and lysozyme activity. Deficient candidacidal activity may place certain cancer patients at high risk of developing systemic candidiasis.

- 2462 STUDIES CONCERNING THE REGIONAL LYMPH NODE IN CANCER. (E.) Fisher, B. (U. Pittsburg Sch. Med., Pa.) and E. R. Fisher. *Cancer* 27(5):1001-1004, 1971.

The popliteal and lateral lymph nodes were removed from the left hind legs of female strain C3HeB/FeJ mice 7 days prior to implantation of an immunizing extract from a spontaneous C3H mammary carcinoma in the left hind leg. Seven days after tumor implantation, the treated legs were amputated and 3 wk after amputation mice were challenged with 10^4 viable tumor cells from the tumor used for immunization. Removal of lymph nodes prior to implantation of tumors resulted in a failure of animals to develop sinecomitant immunity; when lymph nodes remained intact, sinecomitant immunity was manifested. By wk 12 after tumor cell challenge, 53% of mice with lymph nodes removed and 32% of animals with lymph nodes intact had developed tumors. Animals with tumors growing for 28 days in the absence of regional lymph nodes failed to develop concomitant tumor immunity to the same degree as animals with tumors and intact regional nodes. In the former group, tumor incidence amounted to 64% and in the latter group, tumor incidence amounted to 30%.

- 2463 ANTIBODY TO EPSTEIN-BARR VIRUS IN AMERICAN PATIENTS WITH CARCINOMA OF THE NASOPHARYNX. (E.) Goldman, J. M. (Massachusetts General Hospital, Boston), M. L. Goodman and D. Miller. *Jama* 216(13):1618-1622, 1971.

- 2464 TRANSFER OF TUMOR IMMUNITY WITH RNA. (E.) Pilch, Y. H. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), K. P. Ramming and F. Deckers. *Israel J Med Sci* 7(1):246-258, 1971.

- 2465 EVIDENCE OF THE PARTICIPATION OF DEOXYRIBONUCLEIC ACID IN LATE IN CANCER IMMUNITY. (E.) Vlcek, J. (Inst. Radiation Hygiene, Prague, Czechoslovakia), A. Reif and B. Seidlova. *Z Naturforsch* 26(5):414-424, 1971.

- 2466 IMMUNOSUPPRESSION: A PARANEOPlastic SYNDROME. (Ger.) Nagel, G. A. (Basel Univ. Clin., Switzerland). *Schweiz Med Wschr* 101(13):474, 1971.

See also:

- * (Rev): 2158, 2159, 2160, 2172
- * (Chem): 2188, 2226, 2238
- * (Viral): 2295, 2303, 2312, 2323, 2334, 2346, 2347, 2349, 2356, 2360, 239

PATHOGENESIS

67 CHROMOSOMES OF PRECANCEROUS LESIONS OF THE CERVIX UTERI: NEW DATA AND A REVIEW. (E.)
 Riggs, A. I. (Churchill Hosp., Oxford, England),
 E. Bowey and R. H. Cowdell. *Cancer* 27(5):1239-1254,
 1971.

ne biopsies were made on the anterior and posterior
 ects of the cervix uteri of 28 patients with
 eplasia, carcinoma *in situ* and microcarcinoma of
 e cervix; cytogenetic examinations were performed
 the biopsy material. In some cases it appeared
 at the same cell clone was present on both aspects
 the cervix; in these cases an abnormal chromosome
 mber or a distinctive marker chromosome was seen
 both samples of biopsy material. In 2 cases the
 esence of marker chromosomes on opposite sides of
 e os made the relatedness of the 2 cell clones
 equivocal. One of these cases involved severe
 cervical dysplasia with no invasion and the other
 involved severe dysplasia and carcinoma *in situ*.
 e biopsy material showed wide variation in chromo-
 me counts, which grouped at or below 46, in the
 85 region or near 92. Populations with counts in
 e 75-89 region occurred only in cervixes affected
 th microcarcinoma or with *in situ* carcinoma. Nor-
 al diploid cells were rare and marker chromosomes
 re found in 7 of 9 cases of microcarcinoma and in
 of 18 cases of non-invasive carcinoma. No chromo-
 al disorder or marker chromosome was distinctive
 any of the clinical conditions observed.

8 MICROSPECTROPHOTOMETRIC DETERMINATIONS OF
 PROTEIN SULFHYDRYL GROUPS IN THE EPITHELIUM
 ENDOMETRIAL GLANDS IN HYPERPLASIA AND CANCER.
 s.) Kazantseva, I. A. (Inst. Human Morphol., Acad.
 . Sci., Moscow, U.S.S.R.) and N. P. Krut'kovskaya.
 11 *Eksp Biol Med* 71(3):79-81, 1971.

rospectrophotometry of material obtained from 20
 ometrial smears (of 5 healthy women, during the
 0th day of the menstrual cycle, 5 women with
 ndular cystic hyperplasia, 5 women with adenoma-
 s hyperplasia and 5 women with adenocarcinoma) was
 ormed to determine the variations in protein SH
 up levels. The concentration in SH groups
 ressed in relative optical density was 0.14-0.17
 the cytoplasm of normal or glandular hyperplastic
 ometrial epithelium and 0.21-0.28 in that of
 omatous hyperplasia or adenocarcinoma of the
 ometrium. The nucleoli and the nuclei had 0.33
 0.21 optical density concentrations of SH groups,
 ., in adenocarcinoma and 0.20 and 0.14, resp., in
 omatous hyperplasia and glandular cystic hyper-
 sia. The concentration of protein sulfhydryl
 ups was almost the same in the nucleus and cyto-
 sm and only slightly higher in the nucleolus of
 al endometrial epithelial cells. Decreases of
 nucleus/cytoplasmic ratio were also observed,
 , 0.88 in glandular cystic hyperplasia; 0.63 in
 omatous hyperplasia and 0.64 in adenocarcinoma
 pared to 0.98 in normal cells. The significant
 ges in the normal concentration of protein sulf-
 yl groups in the nucleus and cytoplasm of epithel-
 cells in precancerous hyperplasia and carcinoma
 the endometrium appear to be one of the reasons

for the increased number of metaphases and the marked
 increase in the number of pathological mitoses.

2469 THE GROWTH HORMONE IN PATIENTS WITH CANCER
 OF THE UTERUS AND OF THE MAMMARY GLAND:
 ITS RESISTENCE TO GLUCOSE SUPPRESSION. (Rus.)
 Bobrov, Yu. F. (N. N. Petrov Sci. Res. Inst. Oncol.
 Leningrad, U.S.S.R.), S. V. Patokin and V. M.
 Dil'man. *Vop Onkol* 17(3):40-44, 1971.

Growth hormone (GH) levels in blood samples decreased
 1 hr after 1.5 g/kg glucose intake by 37% in 13
 27-yr-old control subjects and by 43% in 13 40-yr-
 old subjects; serum GH and FFA increased by 50% in
 14 middle-aged (53-yr-old) subjects, by 43% in 9
 patients (47-yr-old) with mammary gland cancer and
 by 5-14% in 17 patients (50-58-yr-old) with uterine
 cancer. FFA levels decreased by 45% in the young
 control group, by 10% in the middle-aged group and
 by 16% in patients with uterine cancer. The alter-
 ations in GH suppression by glucose under the
 experimental conditions appeared to be more manifest
 in patients with mammary gland tumor than in those
 with uterine cancer, although alterations of carbo-
 hydrate metabolism occur more often in the latter.
 The loss of GH control appeared to be a result of
 an increase of the hypothalamic threshold for glu-
 cose regulation; such an increase may induce a set
 of metabolic alterations specific to ageing weight
 gain, prediabetes, hypercholesterolemia, athero-
 sclerosis and to conditions promoting neoplasia.

2470 ENZYME HISTOCHEMICAL OBSERVATIONS IN VARIOUS
 FUNCTIONAL PHASES AND IN PATHOLOGICAL
 CHANGES. (Ger.) Bässler, R. (Inst. Pathol., U.
 Mainz, Germany). *Acta Histochem Suppl.* No. 9:605-
 612, 1971.

Histochemical and electron microscopic studies show
 that the administration of estrogens, progesterone
 and prolactin to young female rats elicits
 increased enzyme activities in the mammary epithelial
 cells reaching maximal levels 5 days after treatment
 and plateauing at constant values thereafter. Estro-
 gen treatment produced the most pronounced effects.
 Marked changes were seen in the phosphatases, dehydro-
 genases, nonspecific esterases, ATPase, monoamineoxi-
 dase and 5'-nucleotidase. During lactation, exogenous
 hormones elicited markedly higher enzyme activities
 than those seen during pregnancy or the involutinal
 phase. Topochemically, the phosphatases were selec-
 tively localized in the cell membrane and in the basal
 folds of the glandular epithelium. The increased
 activities of alkaline phosphatase in human mammary
 gland and mammary gland carcinoma tissues (according
 to available data) were considered to be estrogen-
 induced.

2471 LIVER CANCER IN RATS WITH DIETARY CIRRHOSIS.
 (Rus.) Volgarev, M. N. (Natr. Inst. Acad.
 Med. Sci., U.S.S.R., Moscow). *Arkh Pat* 33(2):38-43,
 1971.

Of a total of 262 heterozygotic male rats divided into 4 experimental groups and feed 3 different types of cirrhosis-inducing diets deficient in proteins and the methionine and choline, 73 animals developed histopathologically confirmed hepatic cirrhosis at the end of eleven months. Thirty-four of these 73 cirrhotic rats were then transferred to a completely balanced nutritional diet for periods of 4-15½ months; hepatic cell carcinomas developed in 5 of the 34 rats; it is emphasized that only the cirrhotic rats transferred to a nutritional diet developed liver carcinomas and that none of the animals maintained on the cirrhosis-inducing diets developed neoplasms.

- 2472 THE RELATIONSHIP BETWEEN LUNG CANCER AND TUBERCULOSIS. (Rus.) Rabukhin, A. Ye. (Central Postgrad. Med. Inst., Moscow, U.S.S.R.) and M. Z. Upiter. *Vop Onkol* 17(3):24-32, 1971.

Epidemiological and pathogenic aspects of the relationship between tuberculosis and malignant neoplasia of the respiratory system are discussed. From data accumulated between 1967-1969 in several clinical units of Moscow, the incidence of malignant neoplasia appears to be 4-4.5-fold higher among male tuberculosis patients above 50-yr-old compared to the normal population. Of 161 patients with coexisting lung tuberculosis and cancer, 2/3 seem to have developed neoplasia from various preceding alterations of the pulmonary tissue such as calcification foci of meta-tuberculous scleroses. Of 370 patients with neoplasia, confirmed by fluorography, 112 (30%) exhibited various alterations of tuberculous nature: 1.8% had an active focal process; 18.4% had focal fibrotic or sclerotic alterations of the lung; 9.8% had calcifications within the lymphatic nodes of the chest. Among the patients with monolobular tuberculosis 61% developed homolobular neoplasia and 30% developed homosegmental neoplasia. The role of tuberculosis as a process causing chronic trauma and as a specific carcinogenic factor is reviewed.

- 2473 THE PATHOGENESIS OF PULMONARY CARCINOMATOUS LYMPHANGIOSIS. (Ger.) Schermuly, W. (Surg. Clin., Marburg Univ., Germany) and D. Schaefer. *Strahlentherapie* 141(5):508-517, 1971.

The development of metastases from pulmonary tumors, particularly in the case of lymphangiosis, was investigated and an attempt was made to reconstruct the metastasizing pathways by means of comparative pathological and X-ray findings. Such pathways were traced between 11 hilifugal and 12 hilipetal processes and the lymphangiosis. In one case the lymphangiosis was shown to originate from a single metastatic round focus and in 4 cases from a peripheral pulmonary tumor. A diffuse lymphangiosis possibly derived from a hematogenic carcinoma, developed metastases in all the pulmonary sections.

- 2474 INITIATION OF MALIGNANT TRANSFORMATION AND THE SIGNIFICANCE OF CHANGES IN TRANSFER RNA METHYLASE ENZYMES. (E.) Pillinger, D. J.

(Christie Hosp., Manchester, England) and R. Wilkinson. *Cancer Res* 31(5):630-632, 1971.

Syrian hamster kidney cell lines (normal, spontaneously transformed, and an established tumor line agar plating efficiencies of 2.3%, 15% and 38% resp.) were used to prepare a nonparticulate supernatant fraction for soluble cell component extraction to study the ability of this fraction to incorporate methyl groups from S-adenosyl-L-methionine-methyl-¹⁴C into methyl-deficient *Escherichia coli* tRNA. Spectrophotometric radioactivity assay revealed a 2-fold elevation of the enzymes extracted from the established tumor cell over the normal cells and a less marked elevation in the spontaneously transformed cell line. Morphologically normal cells injected into hamsters at the time of the assay subsequently produced malignant transplantable tumors, indicating a similarity in the methylase enzymes between morphologically normal but tumor-producing hamster kidney cells and the recognizable transformed cells.

- 2475 SERYL TRANSFER RNA CHANGES DURING ESTROGEN-INDUCED PHOSVITIN SYNTHESIS AND UNIQUE SERYL TRANSFER RNA MODIFICATION. (E.) Pick, M. R. (Stanford U. Sch. Med., Cal.) and Mäenpää. *Cancer Res* 31(5):684-687, 1971.

The serine acceptance of hepatic tRNA prepared from estrogen-treated roosters that synthesize phosphovitin (a yolk protein containing greater than 50% serine residues which are nearly all phosphorylated) at a rapid rate was more than 25% greater than that of hepatic tRNA from control roosters. Major differences were seen with seryl-tRNA when the labeled hepatic aminoacyl-tRNA's from control and estrogen-treated animals were compared. Seryl-tRNA from estrogen-treated animals was enriched in 1 major and in 1 minor peak, but no significant differences were observed with the other aminoacyl-tRNA's. The changes in seryl-tRNA correlated with changes in plasma phosphovitin. The seryl-tRNA peaks were characterized by examination of their amino acid composition and their codon response. Paper chromatography products of deacylation revealed that all products contained serine but that the product of peak 4 contained O-phosphoryl-L-serine. Peak 4 was found to contain a unique tRNA^{Ser} species for phosphoserine. Three of the 4 serine tRNA peaks responded to the known serine codons, but peak 4 did not respond and showed only slight binding to poly (U,C). This unusual aminoacyl tRNA may have a unique function in metazoan cellular regulation.

- 2476 PLASMINOGEN ACTIVATOR OF THE BLOOD VESSELS IN TUMOURS AND IN CARRAGEENAN-INDUCED GRANULOMAS. (E.) Pick, C. R. (Dept. Pathology, U. Cambridge, England) and D. B. Catcott. *Brit J Exp Path* 52(1):14-22, 1971.

Cryostat sections of tumor or granulomas from hamsters and mice were incubated on fibrin-covered slides containing plasminogen or no plasminogen from 1

more hr. Fibrinolysis was localized in human and at tissue around mature and small vessels in the stroma which reacted to the invading cancer cells. Fibrinolysis was seen in the plasminogen-free control slides. Systemic injection of inflammatory agents had no effect on fibrinolytic activity of the vessels.

2477 GLYCOLIPID SYNTHESIS IN NORMAL AND TRANSFORMED ANIMAL CELLS. (E.) Robbins, P. (Imperial Cancer Res. Fund, London, England) and J. A. Macpherson. *Proc Roy Soc Lond* 177(1046):49-58, 1971.

The incorporation of ^{14}C -labeled palmitate-1 into cellular lipids was measured in normal and transformed hamster cells *in vitro* to investigate the synthesis of glycolipids in these cell systems. Ceramide monohexoside, ceramide dihexoside and hemasphingoside were present in comparable amounts in normal and in transformed cells; however, 3 larger glycolipids, namely an unknown ceramide which generated

ceramide dihexoside on partial acid hydrolysis (CX), ceramide tetrahexoside (AGL) and ceramide trihexoside (CTH), were consistently absent from transformed cells. In actively growing untransformed hamster cells CX, AGL and CTH were present in smaller amounts than in contact-inhibited hamster cells. It was thought that the disruption of the normal mechanisms of contact inhibition by transformation may have resulted in a lower content of complex glycolipids.

2478 MICROGLANDULAR ENDOCERVICAL HYPERPLASIA ASSOCIATED WITH ORAL CONTRACEPTIVES. (Ser.) Damjanov, I. (Zagreb Med. Inst., Yugoslavia). *Liječnički Vjesnik* 92(9):1049-1054, 1970.

See also:

- * (Rev): 2161, 2163, 2165
- * (Chem): 2189, 2220, 2246

- 2479 THE RISING INCIDENCE OF CANCER OF THE PANCREAS--FURTHER EPIDEMIOLOGIC STUDIES. (E.) Krain, L. S. (Los Angeles, Calif.). *J Chronic Dis* 23(10-11):685-690, 1971.

The incidence and distribution of cancer of the pancreas was investigated in a survey of cases recorded in the California Tumor Registry. The number of observed cases of pancreatic cancer recorded from public county hospitals was 784 among males compared to an expected number of 666 cases; on the other hand, the numbers of observed and expected cases of pancreatic cancer among male patients in private hospitals were 849 and 967, resp. A high incidence of pancreatic cancer was found among Negroes; the incidence in the Negro population in the study was 13 cases/100,000 population for males, while incidences for white and Chinese males were 9.6 and 11.1 cases/100,000, resp. The high Negro incidence did not explain the rising annual incidence of pancreatic cancer mortality in the United States, which has amounted to 300% since 1920. Some etiological factors which may be associated with the increased mortality are smoking, alcoholism and occupational exposure to carcinogens.

- 2480 CARCINOMA OF THE ENDOMETRIUM: A STUDY OF CHANGING RATES OVER A 15-YEAR PERIOD. (E.) Christopherson, W. M. (U. Louisville School Med., Ky.), W. M. Mendez, J. E. Parker, F. E. Lundin and E. M. Ahuja. *Cancer* 27(5):1005-1008, 1971.

The incidence of endometrial carcinoma was investigated among the female population of the Louisville-Jefferson County area in Kentucky during the period 1953-1967; during the study period there were 707 histologically proven cases of adenocarcinoma of the endometrium, with an average incidence rate of 23.8 cases/100,000 population for women 20-yr-old and above. The rate of incidence for endometrial carcinoma among Caucasian women was 52% higher than the rate for Negro women for all women under 70-yr-old; among women 70-yr-old or over, the rate among Negroes was higher than the Caucasian rate. The risk of developing endometrial carcinoma was found to be 4 times higher for women 60-yr-old or more than for women 20-60-yr-old. The average age of endometrial carcinoma patients was 59.6-yr-old for Caucasian women and 64.4-yr-old for Negro women. When average yearly endometrial carcinoma rates from the period 1953-1955 were compared with the rates from the period 1965-1967, a 26.3% increase in incidence was found; however, the increase was not statistically significant when the incidence rates were corrected for aging of the population.

- 2481 EPIDEMIOLOGY OF MALIGNANT MESOTHELIOMA IN HAMBURG: A PRELIMINARY REPORT. (E.) Bohlig, H. (Munic. Hosp., Lubdenscheid, Germany), A. F. Dabbert, P. Dalquen, E. Hain and I. Hinz. *Environ Res* 3(5/6):365-372, 1970.

More than 250 cases of diffuse malignant mesothelioma involving the possibility of occupational, urban or

residential exposure to asbestos dust were found record in Hamburg (1,860,000 population) between 1958 and 1968. Of these 250, 119 case histories were provided with residence and occupational data; the other cases were lacking either occupational residential exposure information and 60 cases had no data on smoking habits. Of the 119 cases, 10 patients lived within the urban area, including mesotheliomas detected in the district of Berged surrounding an asbestos factory. Occupational exposure to asbestos could be ascertained in 54 of the 119 cases; 12 were specifically asbestos workers, 17 were shipbuilding workers. The latency period for the development of mesothelioma appeared to be 10 yr longer (40 yr) in shipyard workers than in workers involved in asbestos factories (30 yr). Urban exposure to asbestos was apparently associated with dust emission from asbestos processing industries which have been brought under control during the last 20 yr.

- 2482 LUNG CANCER IN THE URBAN ENVIRONMENT. (Rus.) Fershtudt, V. I. (Inst. Exper. Clin. Oncol. Acad. Med. Sci., U.S.S.R., Moscow). *Klin Med* 48(12):52-55, 1970.

A retrospective epidemiological study based on certificates and medical records, of lung cancer mortality in Moscow during the years 1958-1959, 1962 and 1964-1965 shows a significant and general continued increase in lung cancer deaths. In 1958 the number of lung cancer deaths in males was 7 compared to 25.3% in 1959; in females, the respective figures were 4.3% and 7.3%. In 1965, male lung cancer deaths were 28%, female rates 7.3%. Lung cancer mortality was increased at age 40 for males and at age 50 for females. Even though the mortality for both sexes in the 50-59 age group was somewhat higher in 1961-62 than in 1958-59, in 1964-65 there was a significant increase in the number of male deaths in all age groups as compared to the mortality in previous years (1958-59, 1961-62). The increase in lung cancer cannot be attributed to improved diagnostic techniques since a comparable increase has not been observed in females. Standardized mortality rates per 100,000 population in various districts of Moscow indicate a higher lung cancer death rate among males living in industrialized areas; in 10 of these districts the male mortality rate is 1.5 times higher than in females. A preliminary analysis of 4 districts shows that male lung cancer victims are significantly more exposed to the effects of industrial pollutants than are females.

- 2483 LYMPHOGRANULOMATOSIS IN CHILDREN OF THE BULGARIAN PEOPLE'S REPUBLIC (1960-1964). (Rus.) Doncheva-Strateva, N. (Postgrad. Med. Inst., Sofia, Bulgaria). *Vop Onkol* 17(3):33-35, 1971.

During the period 1960-1964, an average annual incidence of malignant neoplasia of 15.6/100,000 was reported in children in Bulgaria. Lymphogranulomatosis constituted 7.8% of these cases and appeared to have the lowest incidence among the various types of malignant neoplasms.

cies with an average of 1.2/100,000 (1.5 for boys and 0.9 for girls). The highest incidence of this disease occurred at the age of 10-14 yr (2.1/100,000 for boys and 1.0/100,000 for girls). In early childhood, a peak incidence of 1.8/100,000 at age 4 yr in boys and 0.9/100,000 at the age 3 yr in girls was noted. The incidence of lymphogranulomatosis seemed to be higher for boys in urban areas and for girls in rural areas; however, the differences were not significant.

2485 EPIDEMIOLOGY OF MALIGNANT TUMOURS WITH SPECIAL REGARDS TO THE OROFACIAL REGION.

(E.) Svejda, J. (Pac. Med., J. E. Purkyne U., Prague, Czechoslovakia) and V. Kosut. *Neoplasma* 22:193-196, 1971.

A survey of cancer incidence statistics compiled in Czechoslovakia since 1959 indicated that the oral cavity and liver were affected twice as often among women as among men in that country. Tumors of the larynx and lungs were more prevalent in males than in females. Tumors of the orofacial region were more common among men than among women; in 1968, there were 676 cases of orofacial cancer among men and 188 among women. "Orofacial tumors" as a nosological entity included tumors of the lip, tongue, salivary glands, base of the oral cavity and other parts of the oral cavity. Of these sites, the most commonly affected was the tongue (6455 cases since 1959) followed by the salivary glands (1084 cases), other parts of the oral cavity (923 cases) and the tongue (825 cases). The incidence of orofacial cancer has declined in Czechoslovakia since 1959; in 1958 orofacial tumors accounted for 3.91% of all tumors and in 1968 they accounted for 2.30% of all tumors. This decline was attributed to improved standards of oral hygiene in Czechoslovakia and to increased availability of dental care. Carcinoma of the lip was found to be more frequent in Czech men than in women and to be twice as common in Slovak regions of the country than in Czech regions. This differential prevalence in the 2 sections of Czechoslovakia was thought to be due to differing climatic and geological conditions and to the different age-structure of the populations of the different regions.

2486 TUMORS OF THE NERVOUS SYSTEM: INCIDENCE AND POPULATION SELECTIVITY. (E.) Leib-

man, U. (Hadassah-Hebrew U. Hosp., Jerusalem, Israel), M. Yablonski and M. Alter. *J Chronic Dis* 10(11):707-721, 1971.

The incidence and distribution of nervous system tumors in the Israeli population during 1961-1965 was studied. A total of 1,354 nervous system tumors were recorded. The annual incidence of these tumors was found to be stable, and the incidence of nervous system tumors ranged from 11.1-14.2 cases/100,000 population. Seventy-six percent of nervous system tumors were situated in the brain; of these 50% were located in the cerebellum. Seven percent of nervous

system tumors affected the spinal cord and 12% affected the peripheral nerves. There were 372 gliomas, 236 meningiomas and 159 neuromas and neurofibromas. The male-female ratio for incidence of gliomas was 1.5 and for meningiomas was 0.6. The total male-female ratio for all nervous system tumors was 1.2. Most nervous system tumors had a higher incidence among European-born Israelis than among Asian-born, African-born or native-born Israelis. Gliomas and pituitary tumors, however, were more frequent among native-born Israelis than among the other 3 groups. Although the mortality and morbidity rates for brain tumors in Israel were well above those for other areas, this excess probably reflects the thoroughness of tumor reporting in Israel rather than a real excess of tumor incidence in that country.

2487 THYROID CARCINOMA IN THE JAPANESE IN

HAWAII. (E.) Fukunaga, F. H. (Kuakini Hosp., Honolulu, Hawaii) and L. J. Lockett. *Arch Path* 92(1):6-13, 1971.

One hundred consecutive autopsies performed on persons of Japanese birth or ancestry in Honolulu disclosed 24 cases of occult thyroid carcinoma; in no case was the thyroid carcinoma the cause of death. Among men, 10 Hawaii-born and 6 Japan-born persons had thyroid carcinomas; among women, 2 Hawaii-born and 6 Japan-born persons had thyroid carcinoma. The finding of 24 thyroid carcinomas in 100 Japanese in Honolulu yielded a prevalence rate for thyroid carcinoma in this population of 24%; the prevalence of thyroid carcinoma among Japanese in Japan who had been exposed to nuclear radiation in the atomic bomb blast of 1945 was 17.8-28.4%. The prevalence of thyroid carcinoma in Philadelphia in a 1969 study was 0.45%. Histological examination of the thyroid carcinomas from the Honolulu group revealed small cell nests resembling parafollicular cells situated between the follicles. It was thought that these cells may have been latent medullary carcinomas.

2488 THE PROBLEM OF GASTRO-INTESTINAL CANCER IN INDIA. (E.) Paymaster, J. C. (Tata

Memorial Centre, Bombay, India) and P. Gangadharan. *The Indian Practitioner* 24(1):7-15, 1971.

Cancer of the esophagus constituted 42% of all gastro-intestinal cancers in India according to records from 24 hospitals reviewed in 1964. It constituted 10% of all malignant neoplasms in males (average age of 53 yr) and 7% in women (average age of 51 yr). The upper third of the esophagus was affected in 20%, the middle third in 55% and the lower third in 25% of cases. The malignant lesions in the upper and middle thirds of the esophagus appeared to be associated with the habit of pan chewing or bidi smoking. Gastric cancer constituted 2% of all malignant neoplasms and 13% of the gastrointestinal tract cancers, with a male to female ratio of 3.4:1; the average age was 55 yr for males and 54 yr for females. Fifty-four percent of these patients had achlorhydria while 5% had hyperacidity. The association between achlorhydria and gastric cancer seemed to pass

through a stage of atrophic gastritis. Ingestion of a considerable amount of smoked or charcoaled food could be ascertained in certain regions with high incidence of gastric cancer. Carcinoma of the rectum affected patients, 32% of whom were below 45 yr of age; the low incidence of colonic cancer in India was attributed to frequent chronic infections with bacillary dysentery, tuberculosis or intestinal parasites, which cause an increased rate of bowel movements. The low incidence of gastric, colonic and rectal neoplasia among the Hindu populations of Gujarat seemed to be associated with their strict vegetarian diet.

2488 CANCER IN SOUTHERN IRAN. (E.) Haghighi, P. (Pahlavi U. Sch. Med., Shiraz, Iran) I. Nabizadeh, S. Asvadi and E. A. Mohallatee. *Cancer* 27(4):965-977, 1971.

The incidence of cancer in the population of Fars Province in Southern Iran during the period 1963-1968 was investigated; 3,295 cases of cancer were diagnosed in the area during this period. The 3 most commonly affected sites among males were skin (15.9% of male cases), digestive organs (16.1% of male cases), and lymphatic and hematopoietic tissues (15.4% of male cases). The 3 most commonly affected sites among females were breast (13.9% of female cases), skin (12.4% of female cases) and cervix (11.0% of female cases). The male:female ratio for cancer incidence at all sites was 1.6:1.0. In females, the 50-55-yr-old age group developed more cancer than any other age group, whereas in males, the most frequently affected age group was the 65-70-yr-old group. Cancer incidence in Fars Province was compared with that in the state of Connecticut, and it was found that cancers of the pharynx, esophagus, stomach, liver, nasal cavities and sinuses, and conjunctiva were more common among younger people in Iran than in Connecticut. The incidence of choriocarcinoma in Fars Province was also markedly higher than in Connecticut.

2489 INTESTINAL METAPLASIA OF GASTRIC MUCOSA IN AUTOPSY MATERIALS IN HIROSHIMA AND YAMAGUCHI DISTRICTS. (E.) Kubo, T. (Fac. Med., Kyushu U., Japan) and T. Imai. *Gann* 62(1):49-53, 1971.

Autopsies were performed on 67 randomly selected subjects from Hiroshima, Japan and on 103 randomly selected subjects from Ube, Yamaguchi Prefecture, Japan to determine the incidence of intestinal metaplasia in these groups; metaplasia was graded from 0 (none) to 3 (many patchy areas of uniform metaplasia). The incidences of metaplasia of various grades in age groups 20-29-yr-old, 30-39-yr-old, 40-49-yr-old, 50-59-yr-old, 60-69-yr-old, 70-79-yr-old and 80-yr-old and over were, resp., 12.5, 33.3, 54.6, 76.5, 87.5, 71.5 and 86.1%. Although metaplasia of grades 2 and 3 was not found in subjects aged 20-39-yr-old, it was found in older subjects, the maximal incidence occurring in the age group 70-yr-old and over (75.8% incidence of the 2 grades). The incidence of intestinal metaplasia in Hiroshima was not significantly

different from that in the Yamaguchi Prefecture; however, the incidence in Hiroshima-Yamaguchi was markedly higher than that in a group of autopsies from Minnesota (the incidence of metaplasia was 25% versus 25% for the 50-59-yr-old age group).

2490 A SURVEY OF ACUTE TOXICITY OF CYCADS AND MORTALITY RATE FROM CANCER IN THE MIYAKO ISLANDS, OKINAWA. (E.) Hirono, I. (Gifu U. Sch. of Med., Japan), H. Kachi and T. Kato. *Acta Paediatr Jap* 29(3):327-337, 1970.

Cancer mortality in the period 1961-1966 was investigated in the population of the Miyako islands (Okinawa); members of this population had subsisted on a diet of cycads for a 3 months period in 1960 when alternative food supplies were damaged by typhoons. Mortality from cancer of various sites among Miyako islanders was compared with mortality in Japan. Records of a total of 1,260 persons subsisting on cycads were examined. The age-adjusted death rate per 100,000 population from stomach cancer among islanders was 28.66, while that among Japanese was 47.02. Stomach cancer mortality was most frequent among persons 69-79-yr-old in the Miyako islands and in Japan. The death rate from hepatoma among islanders was 8.89 deaths/100,000 population, while the hepatoma death rate among Japanese was 8.84 deaths/100,000 population. However, in 2 districts of the Miyako islands the death rate from hepatoma exceeded the hepatoma death rate in Japan. No significant increase in deaths from malignant tumors generally was seen in the Miyako islands during 1961-1966. The death rate from cirrhosis of the liver was higher among the Miyako islanders than among Japanese (18.8 versus 10.10 deaths/100,000 population, resp.).

2491 EPIDEMIOLOGIC CHARACTERISTICS OF CANCER OF THE BREAST IN TAIWAN. (E.) Lin, C. (Coll. Med., Natl. Taiwan U., Taipei), K. P. Chen and B. MacMahon. *Cancer* 27(6):1497-1504, 1971.

The incidence of breast cancer in Taiwan was investigated in interviews with 213 breast cancer cases diagnosed in 1964-1967. The overall age-specific incidence rate in Taiwan for breast cancer was 10.1 cases/100,000 female population; the frequency of breast cancer increased with age until the age of 40 yr, at which time it began to decline. Breast cancer mortality in Taiwan increased steadily with age throughout life. In younger age groups, mortality had an appreciably lower frequency than incidence. Persons who had been born in mainland China had a higher death rate from breast cancer (5.1 cases/100,000) than persons born in Taiwan (3.8 cases/100,000); incidence rates for Taiwanese and mainlanders were 6.5 and 19.7 cases/100,000, respectively. Duration of schooling as an index of socioeconomic status, it was found that persons of high social position had high incidences of breast cancer; however, these differences between high and low socioeconomic position were not statistically significant. Single women were found to have high

incidence rates for breast cancer than married women; the death rate among women 40-49-yr-old was 15.1 for single women and 6.8 for married women. A strong inverse relationship was found between parity and incidence of breast cancer; women who had 2 or more births had 30-40% of the breast cancer risk of nullipara. The association with parity was stronger for older women than for younger women. No clear relationship was seen in Taiwan between incidence of breast cancer and age at first pregnancy; no evidence is forthcoming that breast cancer was influenced by lactation. Although a noticeably high number of breast cancer cases reported menarche prior to age 12 yr, differences in breast cancer incidence among Taiwanese with differing menstrual histories were not statistically significant.

92 ORBITAL TUMOURS IN AFRICAN CHILDREN. (E.) Templeton, A. C. (Dept. Path., Makerere Univ., Kampala, Uganda). *Brit J Ophthalmol* 55(4):254-261, 1971.

Twenty cases of proptosis in children under 16, caused by orbital tumors examined during 1964-1968, were surveyed histologically. Patients consisted of 14 males and 20 females ranging in age between 1 and 15-yr-old. There were 28 cases of Burkitt's lymphoma (equally distributed among the sexes), 8 cases of retinoblastoma, 6 cases of myelocoele, 6 cases of fibrous dysplasia, and 3 cases of pseudotumor. In the patients with chloroma, the peripheral blood was normal in 2 cases but the bone marrow was leukemic in all cases. Although only 1 case of orbital rhabdomyosarcoma was seen, it was known to be common in Uganda. Both nasopharyngeal carcinoma and anterior myelocoele were more common in Nilotic and Sudanese tribes, while Burkitt's lymphoma was more common in tribesmen from north and north-west Uganda. Most chloroma patients were from the Kampala area, a finding which may have represented a selection bias rather than a real geographical preponderance for this condition. Two tumors, retinal anlage tumor and esthesioneuroblastoma were apparently unique to the orbit, and these 2 cases were reviewed in detail.

93 ADULT HODGKIN'S DISEASE IN UGANDA. (E.) Olweny, C. L. M. (Dept. Med., Makerere Univ., Kampala, Uganda), J. L. Ziegler, C. W. Ward and A. C. Templeton. *Cancer* 27(6):1295-1301, 1971.

Case notes on 26 cases of Hodgkin's disease recorded among adults in Uganda were reviewed; the mean age of the patients was 25 yr (range of 6-60 yr), and there were 24 male cases. There were 18 cases of cervical lymphadenopathy and 10 cases of hilar lymphadenopathy; hepatomegaly and splenomegaly were seen in 28 cases. In a prospective study of 18 adult Ugandan Hodgkin's disease patients, the average age of patients was 39 yr and there were 13 males and 5 females. There were 11 cases of cervical lymphadenopathy and 9 cases of hilar lymphadenopathy; marrow, liver, lung and

skin were affected in 17 cases. Fifty percent of the 18 cases were diagnosed as of the mixed cellular histopathological type and 39% were of the lymphocyte depleted type. The more malignant histopathological types of Hodgkin's disease were found to be more common in Uganda than in the United States.

2494 MULTIPLE MYELOMA IN SPOUSES. (E.) Kyle, R. A. (Mayo Clin., Rochester, Minn.), C. W. Heath and P. Carbone. *Arch Intern Med* 127(5):944-946, 1971.

Four couples of which each spouse developed multiple myeloma are described. Individuals ranged in age from 51-72-yr at the time of diagnosis of myeloma. Patients had been married for 6-41 yr at the time of the diagnosis of myeloma, and the interval between the onset of myeloma in one spouse and its onset in the other ranged from 1 month to 15 yr. In all cases, myeloma was diagnosed in the male spouse before it was diagnosed in the female spouse. Six of the patients had increased serum globulin values and 3 showed Bence Jones proteinuria.

2495 CYTOCHEMICAL POPULATION ANALYSIS OF CELL LINES DERIVED FROM BURKITT'S LYMPHOMA, INFECTIOUS MONONUCLEOSIS, AND ACUTE LYMPHOCYTIC LEUKEMIA. (E.) De Bault, L. E. (U. Iowa Coll. Med., Iowa City), G. Gahrton and G. E. Foley. *Exp Cell Res* 65(1):156-160, 1971.

Mean values for dry mass, total nucleotides, and Feulgen-DNA content were determined in cultures of lymphocytic cells from patients with Burkitt's lymphoma, infectious mononucleosis and acute lymphoblastic leukemia. Dry mass values showed a distribution similar to that seen in typical exponential phase cell cultures; the 3 cell populations examined showed similar values for dry mass; mean dry mass values varied from 8.1-9.6 preestablished relative units. Total nucleotide content in the cells was measured by extinction of UV and the values for the 3 cell populations were similar, indicating the relative predominance of DNA over RNA in the cells. The frequency distribution of DNA content in the cells showed a bimodal pattern similar to that exhibited by other exponentially growing cells in culture. The frequency distribution of total dry mass and total nucleic acid content were more variable between cells than would have been expected in normal cell populations.

2496 LIGHT MICROSCOPIC OBSERVATIONS OF MORRIS HEPATOMAS. (E.) Hruban, Z. (Dept. Path., U. Chicago, Ill.), H. P. Morris, Y. Mochizuki, D. R. Meranze and A. Slesers. *Cancer Res* 31(6):752-762, 1971.

Transplantable Morris hepatomas of varying rates of growth were examined under the light microscope to determine whether growth rate correlated with structure. It was found that hepatomas of rapid growth rate (including 3683, 8994 and 9098) were composed of multicellular laminae and had small cells and abundant mitotic figures; these hepatoma cells lacked glycogen and follicles. Hepatomas of intermediate growth rate (including 7316A, 5123A and 9121) were found to contain tubular and follicular structures. Slowly growing hepatomas (including 9A(2G), 9633 and 6) contained laminae formed of a single cell. Correlations were not perfect; many slowly growing hepatomas had some of the structural properties of hepatomas of more rapid growth rates.

- 2497 GROWTH OF LANDSCHUTZ ASCITES TUMOR CELLS IN MICE AND IN NORMAL, IRRADIATED AND PRE-IMMUNIZED RATS. (E.) Reuter, A. M. (Nuclear Energy Study Ctr., Mol, Belgium) and G. Mattelin. *Z Ges Exp Med* 155(2):98-104, 1971.

In normal BALB/c mice inoculated with Landschütz ascites tumor cells, ascites tumors grew exponentially for 9 days after transplantation, whereas tumor growth was exponential for only 3 days in normal Wistar rats inoculated with tumor cells. Tumor growth was determined by counting ascites cells in the inguinal canal of killed mice at various times after transplantation of tumor cells. The number of recovered ascites cells declined steadily from day 1 after transplantation in rats preimmunized with ascites cells; by day 5, 0.1 cell was recovered from immunized mice for each cell initially injected. In irradiated (750 r, whole-body) rats, ascites tumors grew progressively for 7-8 days, and then declined. In the irradiated rats, 30 ascites cells were recovered for each injected cell at day 7, but by day 9, only 3 cells were recovered for each injected cell. When tritium-labeled thymidine was used to label ascites cells injected into mice and rats, the labeled cells were quickly lost in immunized rats; in irradiated rats, the radioactivity in the cells fell off abruptly for 1 day and declined more gradually thereafter. Mice injected with the peritoneal wash of rats injected with ascites tumor cells developed tumors when the rats had been given the ascites cells less than 120 hr prior to the peritoneal wash extraction; after a longer interval in the rats, the peritoneal wash did not give rise to tumors in mice. Ascites cells from rats exposed to irradiation produced tumors in mice even when the cells had been allowed to remain in the rats for 168 hr.

- 2498 REGULATION OF ADENYL CYCLASE IN HEPATOMAS OF DIFFERENT GROWTH RATES. (E.) Allee, D. O. (Indiana U. Sch. Med., Indianapolis), J. Munshower, H. P. Morris and G. Weber. *Cancer Res* 31(5):557-560, 1971.

Normal rat liver, regenerating liver from partial hepatectomized rats, and liver from 6 lines of Morris hepatoma were assayed for adenylyl cyclase activity; the hepatomas included slowly growing strains (9618-B and 7787), tumors of intermediate growth rate (5123-t.c. and 7288-C) and rapidly growing strains (3924-A and 9618-A₂). Adenylyl cyclase activity was measured alone and in the presence of glucagon or sodium fluoride. Adenylyl cyclase activity was similar in normal rat liver and in hepatomas of varying growth rates; enzyme activity range from 0.07-0.14 $\mu\text{mole/g/hr}$ in normal liver and in hepatoma tissue. Enzyme activity in regenerating liver was similar to enzyme activity in sham-operated liver. Addition of sodium fluoride caused an increase in adenylyl cyclase activity to 0.74-1.30 $\mu\text{mole/g/hr}$ in normal and in regenerating livers; sodium fluoride caused similar but smaller increases in tumor tissue enzyme activity. Glucagon stimulation caused a significant rise in adenylyl cyclase activity in normal and in regenerating tissues. In slowly growing hepatomas glucagon increased enzyme activity by 442%, while in hepatomas of intermediate growth, glucagon increased adenylyl cyclase activity by 200%. In the more rapidly growing hepatomas, glucagon increased adenylyl cyclase activity by 138% (not significantly different from unstimulated liver tissue); in one of the rapidly growing hepatomas there was no stimulation of adenylyl cyclase activity by glucagon.

- 2499 CELL PROLIFERATION AND TUMOR GROWTH IN HEPATOMAS 3924A. (E.) Looney, W. B. (Virginia Sch. Med., Charlottesville), A. A. Mayo, M. Y. Janners, J. G. Mellon, P. Allen, D. Salak and H. P. Morris. *Cancer Res* 31(6):821-825, 1971.

Growth characteristics of Morris hepatoma 3924A were investigated, and it was found that the mean cell cycle for this tumor was 28.2 hr and its volume doubling time, 5.5 days. The T_{G1} mitotic phase of Morris hepatoma 3924A was 15 hr in duration, the T_{G2} phase was 3.4 hr, the T_S was 9.4 hr, and the $T_{G1}+T_{G2}+T_S$ was 0.4 hr. Although the potential doubling time of the tumor was calculated to be 42.8 hr, the actual doubling time was 132 hr. The cell loss factor was found to be 0.67 and the growth fraction was 66%. It was found that blood comprised about 0.5% of tumor material; connective tissue comprised about 18%, necrotic tissue comprised about 13%, and tumor tissue comprised about 68%.

See also:

- * (Rev): 2170
- * (Chem): 2254
- * (Phys): 2282

00 "SPONTANEOUS" NEOPLASTIC TRANSFORMATION
IN VITRO: THE ULTRASTRUCTURE OF THE
ISSUE CULTURE CELL. (E.) Franks, L. M. (Imperial
Cancer Res. Fund, London, England) and P. D. Wilson.
Cancer J 6(6):517-523, 1970.

The ultrastructures of 11 tumor-producing cell lines
and 13 nonneoplastic cell lines derived from strain
BALB and strain C3H mice were compared; tumor-
producing tissues were taken from kidney, lung,
heart, bladder, tongue and spinal cord and nonneo-
plastic tissues were taken from these organs and
from spleen, prostate and peritoneum. All
exams examined showed 2 predominant cell types:
one cell type had a rounded or bladder-shaped nucleus
with a prominent single nucleolus, the other cell
type had a more convoluted nucleus. Both cell types
were thought to have descended from endothelial
cells and vascular pericytes. Cells in 7 of the 11
tumor-producing cell lines studied had cytoplasmic
lipofuscin deposits; however, there were no consistent
morphological differences between tumor and non-tumor
cells. C-type virus particles were found intra-
cellularly in 7 of 11 tumor-producing lines and in
5 of 13 normal cell lines. Cells from young mice and
from aged mice, cells from different transfer genera-
tions, and cells from different mouse strains were
examined without significant morphological differences.

1 EFFECT OF HYPOTHALAMIC LESIONS ON THE
GENESIS OF SPONTANEOUS MAMMARY GLAND TUMORS
IN THE MOUSE. (E.) Bruni, J. E. (U. Western Ontario
Cancer Res. Ctr., London, Canada) and D. G. Montemurro.
Cancer Res 31(6):854-863, 1971.

Male strain C3D2 F₁ mice were forcebred, and virgin
forcebred mice were subjected to anterior or
middle hypothalamic lesions. A number of the mice
with hypothalamic lesions were rendered sterile.
Among intact forcebred mice, the incidence of mammary
tumors by 60 wk after birth was 93%, whereas the
incidence of mammary tumors among intact virgin mice
at this point was 73%. The latent period for tumor
appearance in intact forcebred mice was 227.5 days,
while the latency for tumors in intact virgins was
344 days. Hypothalamic lesions increased tumor
incidence and reduced tumor latency, although the
effect was not so pronounced as in forcebred mice.
Nulliparous mice given anterior hypothalamic
lesions, the tumor incidence at 60 wk was 100%; in
virgin mice given middle hypothalamic lesions the
incidence was 85%; the tumor latency for
nulliparous mice with anterior lesions was 326 days
while that for virgins with middle lesions was 298.6
days. In forcebred mice with posterior or middle
hypothalamic lesions, the tumor incidence was not
significantly higher than in forcebred mice without
lesions.

INCIDENCE OF SPONTANEOUS TUMORS IN CD^(R)-1
HAM/ICR MICE. (E.) Percy, D. H. (Yale U.
Med., New Haven, Conn.) and A. M. Jonas.
Cancer Inst 46(5):1045-1053, 1971.

The development of spontaneous tumors at various
sites was observed in strain CD^(R)-1 mice in the
following age groups: group I, 0-4 months; group
II, 4-8 months; group III, 8-12 months; group IV,
12-16 months; group V, 16-20 months; and group
VI, over 20 months. The minimal tumor incidence
was seen in group I, in which 2 of 258 mice devel-
oped tumors; the maximal tumor incidence was seen
in group VI, in which 19 of 38 mice developed
tumors. Eighteen of 167 mice in group II developed
tumors, as did 30 of 106 mice in group V. In
groups II, III, IV and V, tumors of the lymphoretic-
ular system were the most commonly developed
lesions. Mammary tumors were most common in groups
III, IV and V, and were relatively uncommon in
group VI; in contrast, pulmonary adenomas were more
common in group VI than in younger age groups (5
pulmonary adenomas in group VI as opposed to 4 in
all other groups). Other tumors developed by the
mice included osteogenic sarcomas, hemangiosarcomas
and renal and hepatic tumors.

2503 TRANSFER RNA AND TRANSFER RNA METHYLATION
IN GROWING AND "RESTING" ADULT AND EMBRYONIC
TISSUES AND IN VARIOUS ONCOGENIC SYSTEMS. (E.)
Gallo, R. C. (Natl. Cancer Inst., Natl. Inst. Hlth.,
Bethesda, Md.). *Cancer Res* 31(5):621-629, 1971.

Escherichia coli tRNA was incubated with leukemic
and normal blast cells, fetal tissue and normal and
neoplastic cell lines for determination of concentra-
tion and activity of tRNA methylase. No significant
differences were found in methylases between the
normal and leukemic lymphoblasts, and both possessed
similar growth rates with virtually identical mor-
phology. When methylases were compared at log phase
vs stationary growth phase, the activities were con-
sistently higher in the cells harvested at log phase
whether normal or neoplastic. Extracts of bone
marrow from normal and chronic myelogenous leukemic
(CML) patients not in an acute phase revealed no
significant differences between normal bone marrow
and leukemic bone marrow extracts when the number of
undifferentiated cells were comparable. However, 2
patients in an acute phase CML and 1 patient with
acute myeloblastic leukemia revealed elevated methyl-
ases. Comparison of peripheral blood of normal donors
and chronic lymphocytic leukemic donors revealed
slightly elevated methylases in the leukemic cells,
but the values were much lower than those found in
normal or leukemic blast cells; a 4- to 7-fold
increase in tRNA methylase activity was seen in
both normal and chronic lymphocytic leukemic cells
in response to phytohemagglutinin.

2504 ISOACCEPTING TRANSFER RNA'S IN MAMMALIAN
DIFFERENTIATED CELLS AND TUMOR TISSUES.
(E.) Yang, W.-K. (Oak Ridge Natl. Lab., Tenn.).
Cancer Res 31(5):639-643, 1971.

Isoaccepting transfer RNA (tRNA) from plasma cell
tumors induced by mineral oil in an inbred strain
of BALB/c mice and reticulocytes from 2 inbred strains

of mice (C57BL/6 and C3H/Anf) were characterized by electrophoretic and chromatographic methods. All aminoacyl-tRNA's derived from tumors producing immunoglobulin A or F were similar in the number and positions of the isoaccepting peaks but were in some cases slightly different in the relative quantities of certain peaks except seryl-tRNA, which showed marked differences. The amino acid composition of reticulocyte hemoglobin α chains of C57BL/6 mouse cells revealed glycine, valine, and asparagine at positions 25, 62 and 68, whereas duplex amino acids (glycine/valine, valine/isoleucine, and asparagine/serine) with a ratio of 30/70 were seen at these positions in the chains from V3H/Anf strain. Reticulocytes from C57BL/6 and C3H/Anf showed identical or similar patterns for tRNA's for glycine, isoleucine, methionine, serine, and tyrosine, but showed a marked difference in valyl-tRNA for which low values were found in the C3H/Anf reticulocytes and high values in the C57BL/6 cells. It is not known whether the characteristic tumor isoaccepting tRNA's are related to the altered methylation of tRNA in tumor tissues.

- 2505 TRANSFER RNA SPECIFICITY IN MAMMALIAN TISSUES AND CODON RESPONSES OF SERYL TRANSFER RNA. (E.) Hatfield, D. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.), F. H. Portugal and M. Caicuts. *Cancer Res* 31(5):697-700, 1971.

Transfer RNA was isolated from bovine kidney, liver and brain directly from whole tissue or following the removal of particulate matter, labeled as aminoacyl-tRNA and analyzed by reversed phase chromatography. Differences in methionyl-, arginyl-, and seryl-tRNA elution profiles resulted from fractions from both isolation methods and when compared to profiles from rabbit tissue, the profiles of liver and brain methionyl-tRNA's were comparable; 2 peaks were resolved from arginyl-tRNA of liver compared to 3 peaks from that of rabbit liver. The major differences noted in seryl-tRNA of bovine brain and liver were comparable to those observed in the corresponding rabbit tissues. These differences, also seen in chicken tissue, did not appear to be affected by heating brain and liver at elevated temperatures in the presence or absence of magnesium. Peak I of liver and Peaks I and II of brain responded to AGU and AGC serine codons; Peak II of liver and Peak III of brain responded to UCG; Peak III of liver and Peaks IV and V of brain responded to UCU, UCA and UCC.

- 2506 THE REGULATION OF TRANSFER RNA METHYLATION IN NORMAL AND NEOPLASTIC MAMMARY CELLS. (E.) Turkington, R. W. (Duke U. Med. Ctr., Durham, N. C.). *Cancer Res* 31(5):644-646, 1971.

The activities of 6 base-specific methylating enzymes were assayed in C3H mouse midpregnancy mammary epithelial cells incubated in organ culture on medium containing insulin. Each of these enzymes increases during the developmental period to maintain character-

istic relative activities, and each was induced by insulin in organ culture. A partially synchronous wave of DNA synthesis was observed following increase in the cellular content of tRNA during the G₁ phase in these epithelial cells. Comparisons of these methylases with those found in spontaneous and serially transplanted mammary carcinomas showed that the specific activity of total tRNA methylase is higher in neoplastic than in normal cells without the corresponding increase in the intracellular content of tRNA; this increase involved a marked increase in some enzymes, such as uridine 5-methylase, while other enzymes were not altered. This distortion of the characteristic enzyme profile was associated with the appearance of tRNA guanine 7-methylase, which was not found in normal C3H mouse mammary tissue. The most attractive explanation for the presence of guanine 7-methylase in the neoplastic mammary epithelial cells is that the gene(s) for this enzyme is normally repressed but becomes activated as a consequence of the neoplastic transformation.

- 2507 IN VITRO TRANSFER RNA METHYLATION IN PAIRED NEOPLASTIC AND NONNEOPLASTIC CELL CULTURES. (E.) Gantt, R. R. (Natl. Cancer Inst., Natl. Inst. Hlth., Bethesda, Md.). *Cancer Res* 31(5):609-612, 1971.

A paired cell line, in which a malignant line was derived from the nonmalignant line, was initiated from a minced mouse embryo pool and was serially cultured in suitable media; both cell lines were labeled with methionine and were assayed for tRNA methylase activity. Radioactive profiles in reversed phase chromatography indicated that the labeled methyl group distribution was quite similar in the malignant and nonmalignant tRNAs. However, in one area of the radioactivity profile relationship more methylation of the malignant cell tRNA was noted. Results were confirmed by Dowex 1-formate column chromatography of the hydrolyzed tRNA's which indicated that 2 extra components were contributed by the malignant cell tRNA. Results are consistent with the aberrant methylation hypothesis of neoplasia advanced by other workers.

- 2508 ANALYSIS OF 5-METHYLURIDINE FUNCTION IN THE TRANSFER RNA OF *ESCHERICHIA COLI*. (E.) Björk, G. R. (Dept. Biol. Sciences, Purdue Univ., Lafayette, Ind.) and F. C. Neidhardt. *Cancer Res* 31(5):706-709, 1971.

Induced mutational defects in genes controlling specific methylation activities were used to compare isogenic pairs of methylation-defective and nondefective strains of *Escherichia coli* mutants to compare growth rate, polypeptide chain growth rate, cell size, and macromolecule composition as well as the relative activity of selected enzymes. Analysis of RNA that was methylated revealed that 6 mutants accepted methyl groups *in vitro* into tRNA, 3 accepted them into rRNA, and 1 accepted them into both. Those accepting methyl groups into tRNA only lacked 5-methyluridine to different degrees in the tRNA, and the mutants

accepting methyl groups into rRNA did so by forming 2-methylguanosine; the mutant accepting methyl groups into both was shown to be a double mutant lacking 1-methylguanosine in its rRNA and 5-methyluridine in its tRNA. Three mutants accepting methyl groups solely into tRNA were shown to possess a gene between minutes 77 and 82 on the *E. coli* chromosome *trmA*. Growth rates of transductant pairs with a *trmA4* allele caused a 15% reduction in a rich medium and a succinate-minimal medium and a 7% reduction in glucose-minimal medium with no observable reduction in a glycerol-minimal medium. Introduction of the *trmA5* gene into various *E. coli* strains caused the same pattern of growth rate changes, yet failed to effect change in yet another strain.

509 COMPARATIVE TRANSFER RNA METHYLASE CAPACITY IN MOUSE ASCITES TUMORS AND IN THEIR DERIVED TUMORIGENIC AND NONTUMORIGENIC CELL CULTURES. (E.) Dell'Orco, R. T. (Dept. Cancer Res., U. Saskatchewan, Saskatoon, Canada), D. G. R. Blair and J. F. Morgan. *Cancer Res* 31(5):561-565, 1971.

Mouse ascites tumor cells of 2 types (TA3 adenocarcinoma and 6C3HED lymphosarcoma) and tumorigenic and nontumorigenic cultured mouse cells were tested for their ability to methylate transfer RNA (tRNA) of *Escherichia coli* B. The nontumorigenic mouse cells were unable to induce tumors in mice after passage in culture. Cells of the 2 ascites tumors showed different capacities to methylate *E. coli* tRNA; the ascites cells designated TA3 had a 30% greater methylating capacity than did the cells designated 6C3HED. Cell extracts from 9 day TA3 ascites tumors and from TA3 tumorigenic cultured cells showed 50-60% more methylating ability than did extracts from nontumorigenic cultured mouse cells of the same cell line. However, 9-day 6C3HED ascites cell extracts showed no difference in tRNA methylase activity when compared to extracts from 6C3HED nontumorigenic cultured cells. Evidently loss of tumorigenicity in this ascites cell system does not entail altered tRNA methylase activity. In a related experiment, it was found that the tRNA methylase activity of cells from a solid 3-methylcholanthrene-induced tumor in mice was 35% greater than that of normal mouse liver and 80% greater than that of normal mouse lung cells.

510 TRYPTOPHANYL TRANSFER RNA SYNTHETASE FROM LYMPHOCYTES OF HUMAN CHRONIC LYMPHOCYTIC LEUKEMIA. (E.) Tchou, H. P. (U. Miami Sch. Med., Fla.), A. J. Claflin and K. H. Muench. *Cancer Res* 31(5):679-683, 1971.

Purification of tryptophanyl tRNA synthetase from a lymphocyte-rich fraction of peripheral blood of a single patient with chronic lymphocytic leukemia was achieved by column chromatography followed by isoelectric focusing, which revealed an isoelectric point of 5.2-5.3. The enzyme was stable in potassium and sodium phosphate buffers at pH 6.9 in the presence of glycerol and 2-mercaptoethanol at 0° and retained 50% of its original activity after 17 days. Phosphate

buffer inhibited enzymatic activity at 100 mM; optimum ATP concentration was 1-3 mM. The enzyme sedimented as a single, symmetrical peak in sucrose density gradient centrifugation and had a molecular weight of about 90,000.

2511 AGENTS OF MODULATION OF THE TRANSFER RNA METHYLASES. (E.) Kerr, S. J. (U. Colorado Med. Ctr., Denver), O. K. Sharma and E. Borek. *Cancer Res* 31(5):633-636, 1971.

The role of regulatory agents on tRNA methylase activity is discussed. An inhibitor fractionated from extracts of adult mammalian tissues by column chromatography on Sephadex G-25 revealed inhibitory action only when the peak fractions I and II were combined. These were a high-molecular weight fraction, sensitive to trypsin and to heating at 100° for 1 min and a low-molecular weight component, which was not inactivated by heating for 10 min at 100°. Embryonic tissue, a Novikoff hepatoma, a Morris hepatoma and Ehrlich ascites cells were found to contain only the low molecular-weight inhibitor component. Ovariectomy reduced the tRNA methylase capacity in extracts of uteri of ovariectomized animals compared with extracts of uteri of intact animals, and the administration of physiological levels of estradiol *in vivo* restored the tRNA methylase capacity; these results were interpreted as an indication of hormonal regulation of the tRNA methylase inhibitor.

2512 TRANSFER RNA METHYLASE ACTIVITY IN NORMAL RAT LIVER AND SOME MORRIS HEPATOMAS. (E.) Sheid, B. (Dept. Pharmacol., State U. New York, Downstate Med. Ctr., Brooklyn), S. M. Wilson and H. P. Morris. *Cancer Res* 31(6):774-777, 1971.

Six Morris hepatomas were transplanted every 4-16 wk into Buffalo male and female rats and the resultant tissue growths were assayed for tRNA methylase activity. All of the 6 Morris hepatomas revealed higher tRNA methylase activity than liver derived from either normal or tumor-bearing animals, the latter two showing no difference. This increased activity corresponded to the growth rates but not in linear fashion. The overall patterns of tRNA methylation produced by the hepatomas and normal liver appeared to be similar, indicating that increased methylase activity may merely reflect an increase in the overall synthesis of RNA by the tumors.

2513 STUDIES ON SYNTHESIS AND MODIFICATION OF TRANSFER RNA. (E.) Gefter, M. L. (Dept. Biol. Sciences, Columbia U., New York, N. Y.) and E. Bikoff. *Cancer Res* 31(5):667-670, 1971.

Escherichia coli was infected with bacteriophage $\phi 80\text{psuIII}$ into which was incorporated the structural gene for tRNA^{tyr}₄^G. Following infection there was a 7-15-fold net increase in tyrosine tRNA; the

majority of tRNA^{Tyr} synthesized was deficient in 2-methylthio-N⁶-(γ,γ -dimethylallyl)adenosine. Reverse-phase column chromatography revealed that, in the order of elution of the unmodified RNA, Peak I contained adenosine adjacent to the anticodon, Peak II, N⁶-(γ,γ -dimethylallyl)adenosine, and Peak IV, 2-methylthio-N⁶-(γ,γ -dimethylallyl)adenosine. The unmodified RNA functioned in protein synthesis with about a 10% efficiency relative to the fully modified RNA. The interpretation of results is complicated by the fact that the effect of a base sequence change cannot be separated from a structure change.

- 2514 THE ANALYSIS OF MALIGNANCY BY CELL FUSION: II. HYBRIDS BETWEEN EHRlich CELLS AND NORMAL DIPLOID CELLS. (E.) Bregula, U. (Dept. Tumor Biol., Karolinska Inst., Stockholm, Sweden), G. Klein and H. Harris. *J Cell Sci* 8(3):673-680, 1971.

Hybrid cell lines were established by fusing Ehrlich ascites tumor cells taken from the peritoneal cavity of mice with fibroblasts obtained from CBA mouse embryos bearing the T6T6 chromosomal translocation. The tumorigenicity of these hybrids was observed in newborn CBA mice which had been exposed to 400 rads of X-irradiation. All hybrid populations were highly tumorigenic; none of the hybrid clones showed a tumor take incidence of less than 60% when inoculated into mice. Although the modal chromosome number to be expected in a hybrid cell line resulting from the fusion of a modal Ehrlich cell with a fibroblast would be 116, the Ehrlich/fibroblast cells had chromosome numbers which fell short of this number by 15-25 chromosomes. Hybrid cells with chromosome numbers approximating the sum of the numbers of both parent cells could not be obtained. The T6 translocation was the only marker chromosome detectable in the Ehrlich/fibroblast hybrids; nevertheless, it seemed likely that at least some of the lost chromosomes in the hybrids were fibroblast chromosomes. In some cases, the chromosome number of cells of tumors produced by the Ehrlich/fibroblast hybrids were similar to those of the hybrid cells themselves, while in other cases, tumor cells showed a reduced modal chromosome number. All tumors showed progressive reduction in chromosome number on transplantation *in vivo*.

- 2515 HUMAN LEUKEMIC CELLS: INHIBITORY EFFECTS OF ISOLOGOUS AND HOMOLOGOUS HISTONES. (E.) Desai, L. S. (Harvard Med. Sch., Boston, Mass.) and G. E. Foley. *Exp Cell Res* 66(1):1-4, 1971.

The effect of histones isolated from the blood of 2 pediatric patients with acute lymphoblastic leukemia, from the blood of a pediatric patient with infectious mononucleosis, and from the bone marrow of a normal pediatric patient on RNA synthesis in normal human fibroblasts *in vitro* was assessed. RNA synthesis was measured by the uptake of ³H-6-uridine by fibroblasts. Histones from the normal patient and from one of the leukemic patients failed to affect ³H-6-

uridine incorporation into the fibroblasts, but histones from the other leukemic patient and from mononucleosis patient produced drastic inhibition of uridine uptake. Untreated fibroblasts had incorporated 1400 cpm/mg RNA of uridine by 18 hr in culture, whereas fibroblasts treated with histones from one of the leukemic patients or from the mononucleosis patient had each incorporated less than 500 cpm/mg RNA of uridine at 18 hr. Histones from the leukemic patient inhibited RNA synthesis in isologous cells to a greater degree than did histones from cells of the mononucleosis patient. Histones from all donors were found to have similar amino acid composition.

- 2516 CYTOPHOTOMETRIC DETERMINATIONS OF DNA CONTENTS IN PRIMARY TUMORS AND METASTASES. (Ger.) Zank, M. (Path. Inst. Karl Marx U., Leipzig, Germany) and H. Krug. *Arch Geschwulstforsch* 36(4):343-351, 1970.

Cell nuclei from primary tumors and metastases were examined for DNA contents using a scanning recording cytophotometer; material included malignancies of the colon, stomach, prostate, bronchi and larynx obtained within 24 hr post-mortem from 10 patients. The karyograms of the primary tumors were categorized under 3 groups according to the frequency distribution of DNA contents of the single cell nuclei, with no correlation between site, cell morphology or logical features was found. Significant differences in average relative values of DNA levels were found between cell nuclei of primary tumor and metastases in 4 out of 10 carcinomas; DNA levels appeared to be higher in the metastasis of colon and prostate carcinoma (27 and 30 U) than in the primary tumor (23 and 23 U, resp.) and were higher in the primary tumor of the gastric and rectal carcinoma (26 and 28 U) than in the metastasis (16 and 22 U, resp.). These data were reflected in corresponding differences in frequency distributions of DNA levels of the individual cell nuclei. The distinct frequency peak in DNA distribution and of its double values characteristic for the major part of the investigated tumors confirmed the Makino and Sandritter lineage theory of tumor development; these peaks should be considered as DNA-stem lines.

- 2517 ISOLATION AND CHARACTERIZATION OF RNA FROM LYMPHOCYTES OF CHRONIC LYMPHOCYTIC LEUKAEMIA. (E.) Deutsch, A. (Chemical Centre, Uppsala, Sweden) and A. Norden. *Scand J Haemat* 8(2):112-117, 1971.

RNA was isolated from lymphocytes with different responses to phytohemagglutinin from chronic lymphocytic leukemia (CLL) patients. The total content of RNA amounted to 0.2-0.3 mg/10⁸ cells. Most of the RNA was obtained in the first extraction step at pH 7.6, and 5-20% was extracted at pH 9 and 60°C. Centrifugation patterns of RNA from the pH 7.6 extracts from lymphocytes of CLL patients were the same as those from normal subjects (28S, 18S and 4S) in 4 of 11 cases. In the other investigated cases of CLL, gradient profiles were obtained which were

acterized by the presence of large amounts of relatively low molecular weight material or of heterogeneous material spreading over the whole range of 28S-4S region. Gel chromatography, gel electrophoresis and sodium chloride fractionation confirmed gradient centrifugation results; RNA from lymphomas that did not respond to phytohemagglutinin resembled normal lymphocyte and liver RNA, while CLL lymphocytes that responded to phytohemagglutinin gave patterns characterized by smaller proportions of 18S components and larger amounts of either relatively low molecular weight material or of polymeric material (28S-4S).

MODIFIED BASES AND TRANSFER RNA FUNCTION.

(E.) Peterkofsky, A. (Nat'l. Heart Lung Inst., Nat'l. Inst. Hlth., Bethesda, Md.), M. Litman and J. Marmor. *Cancer Res* 31(5):675-678, 1971.

Methyl-deficient tRNAs prepared from *E. coli* were compared to tRNA extracted from organisms grown under normal amino acid-supplemented conditions. A comparison of the elution patterns of methyl-deficient tRNA fully acylated with methionine and same tRNA acylated to only a small extent showed significant differences. The deficient species presented a different codon recognition pattern from normal leucine-tRNA, which was bound to ribosomes equally well in response to copolymers containing either uridine and cytosine or uridine and guanine; deficient species responded much better to the uridine-cytosine polymer. The special initiation functions of formylmethionine tRNA were unchanged by lack of methylated bases.

CHROMOSOMAL PATTERNS IN HUMAN MENINGIOMAS.

(E.) Mark, J. (Inst. Pathology, U. Lund, Sweden). *Europ J Cancer* 6(6):489-498, 1970.

Chromosomal studies were carried out on 12 benign meningiomas; case material was drawn from 12 patients 14-68-yr-old and consisted of predominantly cytological and transitional tumors located in the falx, olfactory groove, in the parietal regions (6 cases), and elsewhere. Most tumors were hypodiploid; the modal chromosome peak was 45. In 75% of the tumors, there were numerical and/or structural aberrations of the G group of chromosomes. About 50% of the tumor cells showed marker chromosomes. Chromosomes C and G were primarily involved in the formation of marker chromosomes; in some cases, marker chromosomes were hidden in C chromosomes and did not appear overtly. It was found that in a group of malignant primary tumors in children the major chromosomal aberrations were found in the G and C groups, as they were in the meningiomas.

PATTERNS OF ISOACCEPTING PHENYLALANINE TRANSFER RNA IN HUMAN LEUKEMIA AND LYMPHOMA.

(E.) Mittelman, A. (Roswell Park Memorial Inst., Buffalo, N.Y.). *Cancer Res* 31(5):647-650, 1971.

Transfer RNA^{Phe} was extracted from fresh, surgically removed spleens from patients with leukemia, malignant lymphomas, and nonneoplastic disease and aminoacyl tRNA synthetase was extracted from spleen and human fetal liver; the tRNA and synthetase were used for assay of amino acid acceptor activity. Attempts to charge tRNA extracted from 3 spleens with a number of amino acids were not successful until the RNA was run through BD-cellulose chromatography. Nonneoplastic spleen accepted RNA^{Phe} only. Transfer RNA extracted from both neoplastic and nonneoplastic spleen exhibited similarities in the pattern of phenylalanine tRNA separation and charging; 2 well-defined phenylalanine-accepting peaks were seen when autologous aminoacyl synthetases were used, and a third isoaccepting tRNA^{Phe}, not previously reported, was found in malignant lymphomas and chronic lymphatic and myelogenous leukemias.

2521 RESPONSE OF MODIFIED PHENYLALANINE TRANSFER RNA TO RECOGNITION BY PHENYLALANINE TRANSFER RNA SYNTHETASE. (E.) Stulberg, M. P. (Oak Ridge Nat'l. Lab., Tenn.) and L. R. Shugart. *Cancer Res* 31(5):671-674, 1971.

Undermethylated *Escherichia coli* tRNA^{Phe} prepared by reversed-phase fractionation was measured for activity and phenylalanine acceptance. Preparation 1 (original) had reduced activity for total phenylalanine acceptance and was highly methylated whereas Preparation 2 (purified from same batch as preparation 1 several yrs and several columns later) as well as preparation 3 (from a new growth of cells) showed significantly reduced activity with the undermethylated preparations demonstrating equal initial velocities at saturating tRNA^{Phe} concentrations. Optical rotatory dispersion spectra of undermethylated and normal tRNA showed great similarity but there was a noticeable divergence in the lower wavelength region in the undermethylated fraction; circular dichroism spectra indicate a deviation from the normal on the rising limb of its absorption curve. Hyperchromicity changes at 260 nm with increasing temperature showed that the undermethylated sample began melting out at the same temperature as the normal preparation but soon deviated from this curve and showed an increased rate of melting out at lower temperatures. Phenylalanine incorporation in response to poly U-stimulation was markedly reduced in the undermethylated fraction.

2522 EFFECT OF SEX ON THE DEVELOPMENT OF MELANOMA IN HYBRID FISH OF THE GENUS *XIPHOPHORUS*. (E.) Siciliano, M. J. (Biol. Dept., Long Island U., Brooklyn, N. Y.), A. Perlmutter and E. Clark. *Cancer Res* 31(6):725-729, 1971.

The incidence of melanoma development was observed in the offspring of matings between the platyfish (*Xiphophorus maculatus*) and the swordtail fish (*Xiphophorus helleri strigatus*); matings were effected by artificial insemination. In some cases

the female partner to the cross was a platyfish, and in some cases a swordtail. Of male offspring of a female platy x male swordtail cross, 88% developed melanoma; the percentage of female offspring of this cross developing melanoma was 55.9%; among offspring of a female swordtail x male platy cross, 78% of the males and 51.6% of the females developed melanomas. By 300 days after birth, 85% of all males had melanoma and 53% of all females had melanoma. The tendency for a higher percentage of males to develop melanoma existed in F_1 generation fish from the female swordtail x male platy cross as well as in the F_1 generation of the reciprocal cross. It was thought that the excess of tumor development among male fish was due to an augmentation of melanotic process by the male sex hormones.

- 2523 TRANSFER RNA AND TRANSFER RNA METHYLASE IN HUMAN BRAIN TUMORS. (E.) Viale, G. L. (Neurosurgical Clin. U. Genoa, Italy). *Cancer Res* 31(5):605-608, 1971.

Tissue from 68 human brain tumors and 6 normal human brains were used for preparation of tRNA and were assayed for methylase capacity. Tumor tissue methylated tRNA 3-4 times more actively than normal tissue irrespective of the type of neoplasm which was the source of the methylases of the tRNA; tumor tissues also contained larger amounts of methylated nucleosides than those from normal brain tissue. Rapidity of growth did not correlate with methylase activity or capacity. Sequential methylation of homologous substrates suggest that a shift in the specificity occurs in tumor material.

- 2524 CHROMOSOME NUMBER ADJUSTMENT IN THE LANDSCHÜTZ MOUSE ASCITES CANCER. (E.) Leonard, A. (Dept. Radiobiol., C.E.N.-S.C.K., Mol, Belgium). *Rev Europ Etud Clin Biol* 16(1):58-61, 1971.

After 7-900 transplantation passages, karyotype studies were performed on cells of a mouse Landschütz ascites tumor. This tumor has a stable stem line of 46 chromosomes and contains 3 minute acrocentrics, 1 having a secondary constriction; the 46th chromosome is a long metacentric. Karyotype studies on passaged Landschütz cells from mice which had been given an i.p. injection of 0.5 cc of an 0.025% colchicine solution showed that the stemline chromosome number had changed from 46 to 44. One of the minute acrocentrics had disappeared; however, the long metacentric and the acrocentric with the secondary constriction were still in evidence.

- 2525 THE CHROMOSOMAL ABERRATION OF DOUBLE-MINUTES IN A HUMAN EMBRYONIC RHABDOMYOSARCOMA. (E.) Granberg, I. (U. Hosp. Inst. of Pathology, U. Lund, Sweden) and J. Mark. *Acta Cytol* 15(1):42-45, 1971.

Biopsy material was collected from an embryonic rhabdomyosarcoma which arose in a 16-yr-old boy; the tumor had been exposed to radiation. Chromosome studies showed that the tumor had a hypotriploid cell stemline. All cells examined contained double-minute chromosomes, the number of double-minutes varying from 3-60/cell. Most cells had less than 10 double-minute chromosomes. Interphase cells showed a relatively high number of micronuclei, suggesting that the double-minute chromosomes behaved irreversibly in mitosis.

- 2526 TRANSFER RNA MODIFICATIONS AND SYNTHESIS IN ANIMAL CELLS. (E.) Taylor, M. (Dept. Microbiol., Indiana U., Bloomington), S. Volkers, B. K. Choe and J. G. Zeikus. *Cancer Res* 31(5):688-693, 1971.

Alterations in chromatographic patterns of specific species of tRNA's have been studied in sea urchin from the time of fertilization to the formation of the late mesenchyme blastula by means of column chromatography of 8 different aminoacyl-tRNA's in unfertilized eggs and mesenchyme blastula and in Morris hepatomas. No elution differences could be found for arginyl-, tyrosyl-, valyl-, phenylalanyl-, aspartyl-tRNA but repeated differences were found chromatographically for leucyl-, seryl-, and lysyl-tRNA. These data suggest that certain species of blastula tRNA's differ from egg tRNA, which must result from modifications of existing tRNA's. Regenerating rat liver and normal rat liver, used as comparisons, demonstrated no detectable differences in reverse phase partition chromatography. However, with 2 hepatomas, classified as highly differentiated and well-differentiated, resp., distinct repeatable differences were found in seryl-, prolyl-, alanyl-, histidyl-, and lysyl-tRNA's but no differences were detectable between a poorly differentiated hepatoma and regenerating rat liver.

- 2527 APPLICATION OF A TRITIUM DERIVATIVE TO HUMAN BRAIN AND BRAIN TUMOR TRANSFER RNA ANALYSIS. (E.) Randerath, K. (Massachusetts General Hosp., Boston). *Cancer Res* 31(5):658-661, 1971.

Unfractionated tRNA isolated from various normal and neoplastic tissues were analyzed for base composition by means of a tritium derivative method. Substantial changes of the minor base composition were found in tumor tRNA when compared to tRNA isolated from normal human brain tissue. There was a slightly higher level of 7-methylguanosine in glioblastoma multiforme than in normal brain tissue. Values for brain tissue resemble reported values for rat liver.

- 2528 MITOCHONDRIAL RIBOSOMES IN HeLa CELLS. (E.) Attardi, G. (California Inst. of Technology, Pasadena) and D. Ojala. *Nature* 229(5):133-136, 1971.

sedimentation properties of the submitochondrial fractions obtained from Triton X-100 lysates of mitochondria from HeLa cells that had been exposed for 2 hr to ^3H -5-uridine in the presence of 0.1 $\mu\text{g/ml}$ actinomycin D were investigated. The A_{260} profile of the sedimentation pattern showed 3 radioactive peaks, 60S, 45S and 35S, as well as an unlabeled 74S peak. The RNA extracted from the peak fraction of the 60S component showed both 16S and 12S species; the RNA from the peak fraction of the 45S peak showed principally a 16S component and some 12S, whereas RNA from the peak fraction of the 35S peak showed mainly a 12S component. These radioactive peaks appear to represent mitochondria-specific mononucleoprotein particles containing 16S and 12S RNA. Reconstruction experiments using purified 12S and 16S RNA with unlabeled mitochondrial suspensions produced no discrete 35S, 45S or 60S peaks from artificial complexing with proteins. That the 60S particles represent mitochondria-specific ribosomes is supported by the inhibition of its synthesis by chloramphenicol and its insensitivity to cycloheximide. The 45S and 35S particles are probably subunits of the 60S ribosomes.

9 ENGAGEMENT OF CYTOPLASMIC POLYRIBOSOMES IN THE SYNTHESIS OF RIBOSOMAL PROTEINS IN EUCARYOTIC CELLS. (E.) Chiarugi, V. P. (Inst. Biol. Path., U. Florence, Italy). *Cancer Res* 31(6): 1185-1190, 1971.

^3H -labeled structural ribosomal proteins were extracted from mouse Ehrlich adenocarcinoma ascites cells and ^3H -labeled proteins were produced by a cell-free system of cytoplasmic polyribosomes. Labeled proteins were subjected to electrophoresis on polyacrylamide gels. C^{14} -labeled ribosomal proteins and ^3H -labeled peptide chains were found to produce congruent electrophoretic patterns among the fast-moving proteins, but the 2 proteins did not show congruent electrophoretic patterns among the slower fractions. When the 2 proteins were examined by carboxymethylcellulose chromatography, both proteins eluted at approximately the same positions. Apparently, a cell-free system from the Ehrlich ascites cells is able to synthesize some proteins which behave chromatographically and electrophoretically as ribosomal proteins.

80 HUMAN LEUKEMIC CELLS: ABNORMAL AMOUNT OF METHYLATED BASE IN DNA. (E.) Desai, L. S. (Harvard Med. Sch., Boston, Mass.), U. C. Wulff and E. Foley. *Exp Cell Res* 65(1):260-263, 1971.

Base ratio and nearest neighbor analyses were determined with DNA isolated from cultures of human leukemic lymphocytes. The hydrolysates of DNA from human lymphocytic cells exhibited patterns similar to those of leukemic lymphocytes with respect to major deoxyribonucleotides, although there seemed to be minor differences in base content, particularly in thymine and guanine. ^3H -L-Methionine-methyl was incorporated primarily into thymine and cytosine, and to a lesser extent, into guanine. An extra small peak which mi-

grated between cytosine and thymine and which had an R_f value identical with that of 5-methylcytosine was seen in DNA derived from patients with leukemia but not in DNA from cells derived from patients with infectious mononucleosis or in normal lymphocytic cells. This distinction between lymphocytes of leukemic and infectious mononucleosis patients, as well as other reported metabolic differences, suggests functional and/or regulatory differences between the lymphocytes which may relate to the manifest biological differences between these 2 lymphoproliferative diseases.

2531 PRIMARY POLYCYTHAEMIA: CORRELATIONS BETWEEN THE HISTOLOGIC APPEARANCES AND THE CHROMOSOME PATTERN OF THE BONE MARROW CELLS DURING THE DISEASE. (E.) Visfeldt, J. (Community Hosp., Copenhagen, Denmark), S. Franzen and B. Tribukait. *Acta Radiol* 10(1):86-114, 1971.

Bone marrow cells and peripheral blood cells from 25 patients with polycythemia were subjected to karyotype studies; patients ranged in age from 22-74 yr and were classified as untreated (4 patients), treated and without bone marrow fibrosis (9 patients), treated and with bone marrow fibrosis (5 patients), and treated and showing incipient transition to leukemia (7 patients). Treated patients had often received radiation. Unstable chromosome aberrations were found mainly in peripheral blood of these patients and consisted chiefly of dicentrics, rings and acentric fragments. No tracentrics were seen and no significant increase in chromatid aberrations was seen in the patients. Most aberrations were explained as deletions. The maximum incidence of aberrations was 91% in treated patients without myelofibrosis, 100% in treated patients with myelofibrosis, 100% in patients with incipient leukemia and 9% in untreated patients. Clone formations were seen in bone marrow specimens from 12 patients.

2532 CYTOLOGICAL AND CYTOGENETICAL STUDIES ON BRAIN TUMORS: III. Ph^1 -LIKE CHROMOSOMES IN HUMAN MENINGIOMAS. (E.) Zankl, H. (Max-Planck Inst. Psychiatry, Munich, Germany) and K. D. Zang. *Humangenetik* 12(1):42-49, 1971.

A survey of 70 human meningiomas revealed 5 having a chromosome resembling the Philadelphia chromosome (Ph^1) previously associated with chronic myelogenous leukemia. Three of the meningiomas were arachnoid, 1 was endotheliomatous and 1 was fibromatous. In 3 tumors having a modal chromosome number of 46 the Ph^1 chromosome could be shown to be a deleted G chromosome, while in the other 2 meningiomas it was suspected but not shown that the G group was the origin of the Ph^1 .

2533 CANCER FAMILY "G" REVISITED: 1895-1970. (E.) Lynch, H. T. (Creighton U. Sch. Med., Omaha, Nebr.) and A. J. Krush. *Cancer* 27(6):1505-1511, 1971.

The incidence of cancer was investigated in members of a family which was seen to have a high frequency of cancer cases when first examined in 1895. The family's "progenitor" had 10 children, of whom 6 developed carcinoma; the descendants of the 10 children were taken as unit groups, and it was found that 8 of the 10 groups were cancer-prone. Investigation of the branches of the family ultimately involved 650 related individuals. In these 650, there were 95 cases of cancer; in the 8 cancer-prone branches of the family, the cancer incidence ranged from 20-62%. Stomach cancer, colonic cancer and endometrial cancer tended to cluster in cancer-prone families, as did leukemia and lymphosarcoma. The sex ratio of males to females in the family who had been affected by cancer approached 1:1.

- 2534 FANCONI'S ANAEMIA IN THE GENETICS OF NEOPLASIA. (E.) Swift, M. (New York U. Med. Ctr., New York). *Nature* 230(5293):370-373, 1971.

Genetic studies in patients with Fanconi's anemia (FA) from 8 families were performed. Lymphocyte cultures from the living probands (belonging to 5 of these families) and cultures previously prepared from a proband who died later showed the specific characteristic chromosomal features. In one of the 8 families the parents were first cousins. Since 1930, 102 deaths of relatives whose prior probability of FA heterozygosity was higher than 0.1 occurred. Malignant neoplasm was the cause of death in 27 cases, and the age of death ranged between 50 and 74 yr. In a normal population 17 deaths from malignant neoplasm would be expected under similar distribution by age and year of death (1952). Of the malignant neoplasms which occurred in the 8 families excluding the probands (372 living relatives), several types of neoplasia occurred with unusually high frequency. Three cases of leukemia were found where 1 would be expected. Two of these cases were in 1 family, acute myeloblastic leukemia in an uncle and acute lymphatic leukemia in a first cousin of an FA proband. There were 5 colonic and 4 gastric carcinomas, while in a normal population perhaps 2 of each would have occurred in 102 deaths. Since it is not possible to distinguish FA heterozygotes from non-carriers in the FA families, there was no way to tell from these data whether specific types of cancer or leukemia were associated with the FA gene. There are no precise estimates of the incidence of FA homozygotes or of the frequency of the FA gene. However, if the FA heterozygotes are about 3 times as likely as non-carriers to die from a malignant neoplasm, (as the data indicate) then they would constitute 1% of all patients dying of cancer or leukemia.

- 2535 TESTICULAR MORPHOLOGY AND GERM CELL DNA SYNTHESIS IN THE TESTIS OF PATIENTS WITH PROSTATIC CARCINOMA. (E.) Markewitz, M. (Francis Delafield Hosp., New York, N.Y.), R. J. Veenema, B. Fingerhut and E. Gursel. *Cancer* 27(4):919-924, 1971.

In biopsy studies of testicular tissue taken from 175 patients with histologically proven carcinoma

of the prostate, it was found that 40-45% of biopsied testicular tissues contained seminiferous tubules with full and satisfactory spermatogenesis. In 35-40%, spermatogenesis was active but depleted. Leydig cells were increased in this second group. In the remaining 20-25%, atrophy and hyalinization were seen. DNA synthesis was found to be reduced in all 3 groups of testicular biopsies from carcinoma patients. No consistent correlation could be found between testicular morphology, DNA synthesis and serum testosterone levels in the patients.

- 2536 MODAL DNA VALUE AND CHROMOSOME NUMBER IN OVARIAN NEOPLASIA. (E.) Atkin, N. B. (Mount Vernon Hosp., Northwood, Middlesex, England). *Cancer* 27(5):1064-1073, 1971.

Chromosome preparations were made from tissue of patients with ovarian carcinoma for modal value and DNA content determination by means of microspectrophotometry. The carcinomas appeared to fall into discrete groups according to their modal chromosome numbers, whether assessed from metaphase chromosome counts or DNA measurements on interphase cells, revealed a low-ploidy and high-ploidy characteristic. The modal values of the high-ploidy tumors covered a wide range, but near-triploid numbers appeared to be favored. The mean ratio of equivalent to actual modal chromosome number for 12 low-ploidy tumor regions was 1.03 compared to 1.05 in the high-ploidy group and 1.10 in the high-ploidy recurrent tumor group. Multiple specimens obtained from 18 malignant tumors showed similar DNA values. No clear difference between the 2 groups with respect to histopathologic type was seen; however, those in the low-ploidy group showed a tendency towards a higher degree of differentiation. Those in which the tumor was confined to one or both ovaries fell mainly in the low-ploidy group; this group showing a significantly better survival rate than those in which there was spread beyond the ovaries.

- 2537 ABNORMAL HORMONE RESPONSES OF AN ADRENAL CORTICAL CANCER ADENYL CYCLASE. (E.) Schorr, I. (Dept. Med., U. North Carolina, Chapel Hill) and R. L. Ney. *J Clin Invest* 50(6):1295-1300, 1971.

Adenyl cyclase was assayed in the subcellular fractions of a corticosterone-producing adrenocortical carcinoma of the rat. Enzyme activity was found in all particulate fractions of normal rat adrenals and tumor tissue. The fractions examined were 1000 g particles, 10,000 g particles and 105,000 g particles. Activity was lowest in the 105,000 g fraction. Adenyl cyclase activity in each of the fractions of tumor normal adrenal was stimulated by ACTH, although responses of the 105,000 g fractions were small. The response of the enzyme to a given concentration of ACTH was usually more pronounced in tumor tissue than in normal adrenals. The lowest effective stimulating concentration of ACTH for malignant and normal tissue was 0.051 U/ml. Sodium fluoride also stimulated adenyl cyclase activity in normal adrenal tissue 8-fold, but had only a small effect on malignant adrenal tissue.

nephrine and norepinephrine stimulated adenylyl cyclase activity in the tumor tissue but not in normal renal tissue. Tumor cyclase was not responsive to angiotensin, vasopressin, glucagon, insulin, growth hormone, parathyroid hormone or thyrocalcitonin.

3 CHROMOSOMAL CHARACTERISTICS OF THE NK/Ly MOUSE ASCITES TUMOUR PASSAGED ON AB/Jena-Ko. STRAIN MICE. (E.) Seidlova, A. (Fac. Natural Sciences, P. J. Safarik U., Kosice, Czechoslovakia) and J. Horak. *Neoplasma* 18(1):19-26, 1971.

Specimens of NK/Ly ascites tumor were removed from AB mice and prepared for chromosome study; tumor had been transplanted to the donor mice and in its 26th passage. Tumor cells in metaphase showed marked aneuploidy, and most of the cells in metaphase were diploid. The modal number of chromosomes was 42. A large telocentric A chromosome with marked achromatic space and a large metacentric chromosome were seen in tumor cell karyotype preparations. Tumor cell metaphases also showed 1-3 minute chromosomes. It was found that 0.93% of tumor cells had spontaneous aberrations (translocations).

THE ENERGY METABOLISM OF NOVIKOFF ASCITES HEPATOMA CELLS: I. THE EFFECTS OF GLUCOSE ON THE INTRACELLULAR LEVEL OF ADENINE NUCLEOTIDES. (E.) J. W. (Mc Gill U. Cancer Res. Unit., Montreal, Quebec, Canada) and P. G. Scholefield. *Canad J Biochem* 49(6):686-694, 1971.

On addition of glucose 5 mM (or mannose) to freshly washed Novikoff ascites hepatoma cells resulted in an increase in the level of high energy nucleoside phosphates. Analysis of changes in the levels of specific adenine nucleotides showed that the decrease in ATP-hydrolyzable nucleotide phosphates was paralleled by a rapid loss of ATP which reached a minimum 1-3 min after the addition of glucose; a 50% decrease in the total adenine nucleotide pool was also observed. Subsequently, there was a constant rate of regeneration for 20-30 min which reached a new steady state in 1 hr; the low constant levels of AMP and ADP during this time suggested that the regeneration of AMP was the limiting step. Thin layer chromatography analysis of acid-soluble fractions of reaction mixtures indicated that 50% of the adenine nucleotide pool was catabolyzed within the first 10 min after the addition of glucose to give mainly hypoxanthine. Hadacidin (0.5 mM or more) inhibited the conversion of hypoxanthine to adenine nucleotides by 25% between 10 min after the addition of glucose; the addition of adenine to the reaction mixture reversed the inhibitory effect of hadacidin, indicating that AMP regeneration was also occurring by the reaction of hypoxanthine with phosphoribosyl pyrophosphate. The phenomenon of ATP depletion which occurs with the addition of glucose to freshly washed Novikoff cells is probably due to utilization of ATP for restoration of electrolyte balance; preincubation of cells in medium to allow restoration of electrolyte balance eliminated the ATP depletion.

2540 DIFFERENCES IN THE *IN VITRO* AMINO ACID LABELLING PATTERN OF MITOCHONDRIA FROM MELANOMA AND LIVER. (E.) Birkmayer, G. D. (Derm. Clin. U. Munich, Germany), and B.-R. Balda. *Febs Letters* 15(2):156-160, 1971.

Mitochondria isolated from 5 livers and 5 tumors of female Syrian hamsters receiving serial s.c. transplantation of an amelanotic hamster melanoma were incubated with various labeled amino acids and subsequently treated with cycloheximide, chloramphenicol and proflavine. The isolated mitochondria of the melanoma incorporated the amino acids at a rate more than 4 times greater than that of the liver mitochondria. Cycloheximide had no effect on label incorporation into the melanoma mitochondria but inhibited this in liver mitochondria. Chloramphenicol produced a 50% inhibition of label incorporation in melanoma mitochondria and a 38% inhibition in liver mitochondria, while proflavine produced no inhibition in the melanoma mitochondria and a 30% inhibition in liver mitochondria. Sonication of melanoma mitochondria in phosphate buffer solubilized about 1/4 of the total radioactivity incorporated and about 60% of the protein, while in liver mitochondria, 45% of the protein and 6% of the total radioactivity was solubilized. The labelling pattern produced at least 3 bands on gel electrophoresis at 2.5 cm, 3.3 cm and 4.0 cm which were radioactive in the melanoma but were unlabeled in the liver mitochondria.

2541 THE TYROSINASES OF MOUSE MELANOMA: ISOLATION AND MOLECULAR PROPERTIES. (E.) Burnett, J. B. (Massachusetts General Hosp., Boston). *J Biol Chem* 246(10):3079-3091, 1971.

The tyrosinase activity in Harding-Passey melanoma maintained by serial s.c. transplantation in Swiss white mice was determined by spectrophotometric or manometric techniques. Two soluble and 1 insoluble fractions of active tyrosinase were obtained; the 2 soluble fractions had molecular weights of 66,000 and 56,700, resp. The amounts of amino acid residues in the 2 fractions of histidine, arginine, serine, glycine, alanine, isoleucine, methionine, phenylalanine, glutamic acid and tryptophan approximated each other in weight, whereas aspartic acid and threonine showed the greatest variation; lysine, proline, half-cystine, valine, leucine, and tyrosine also showed marked variation. These results suggest that the molecule of tyrosinase may be a single chain rather than a multichain protein.

2542 LYSOSOMES IN MOUSE MELANOMA. (E.) Seiji, M. (Dept. Derm., Tohoku U. Sch. Med., Sendai, Japan) and N. Otaki. *J Invest Derm* 56(6):436-440, 1971.

Lysosomal enzyme activities were measured in centrifugation fractions of the B16 mouse melanoma, and correlations between enzyme activity and tumor growth were observed in transplantation experiments with the same tumor. Tyrosinase and succinate dehydrogenase

were confined mainly to the fraction of tumor tissue preparation containing mitochondria, lysosomes and some microsomes. Cathepsin and acid phosphatase were located in this fraction, but were also found in the cell supernatant. In related experiments, the melanoma was transplanted to D-D line mice, 5 of which were killed every 4th day for 29 days. Tumors were resected, weighed and centrifuged at $11,000 \times g$ for 20 min. Nine days after transplantation of the tumor, its weight and size began to increase progressively; the tumors eventually became necrotic, and most mice had died by 29 days after transplantation. Acid phosphatase activity increased from the time of tumor transplantation, and reached its maximum by 5-9 days after transplantation, β -glucuronidase showed a similar course. Cathepsin activity declined from transplantation until day 5, and thereafter increased sharply, and reached its maximum on day 9. An increase in succinate dehydrogenase paralleled the increase in tumor weight until day 21 after transplantation. Tyrosinase activity reached its maximum on day 9. By day 21-29 after transplantation, most enzymes had declined to levels similar to those found at the time of transplantation of the melanoma.

- 2543 ULTRASTRUCTURAL STUDIES OF HARDING-PASSEY MOUSE MELANOMA. (E.) Seiji, M. (Dept. Derm., Tokyo Med. and Dental U., Sch. Med., Japan) and N. Otaki. *J Invest Derm* 56(6) 430-435, 1971.

Hardin-Passey mouse melanomas were serially transplanted to a Swiss strain of mice and were examined by electron microscopy. Three types of cells were revealed: a melanin-producing cell, a melanin-containing cell and a melanin-producing and -containing cell. In the melanin-containing cells, melanosomes in various developmental stages were scattered throughout the cytoplasm. The shape of the melanosomes was roughly spherical and the diameters varied from 0.3 to 0.6 μ . In the melanin-containing cell, melanosomes were present in the form of melanosome complexes. These complexes are believed to be some sort of a lysosome formed by autophagy. The melanin-producing and -containing cell is assumed to be the aged melanocyte and the melanin-containing cell to be the older melanocyte.

- 2544 NUCLEOTIDE POOLS OF NOVIKOFF RAT HEPATOMA CELLS GROWING IN SUSPENSION CULTURE: II. INDEPENDENT NUCLEOTIDE POOLS FOR NUCLEIC ACID SYNTHESIS. (E.) Plagemann, P. G. W. (Med. Sch. U. Minnesota, Minneapolis). *J Cell Physiol* 77(2): 241-258, 1971.

Novikoff rat hepatoma cells were incubated with 3 concentrations of 3H -5-uridine (100, 10 and 0.5 μM) for 20 min followed by washing with warm medium and incubation in fresh medium either free of uridine or containing unlabeled uridine and were analyzed for radioactivity in total cell material and in acid-soluble material. After 20 min of labeling 80-85% of the total label associated with the cells was found in acid-soluble material regardless of the

uridine concentration during the pulse period; however, the washing procedure immediately stopped further incorporation and was followed by a slow constant rate of radioactive loss during the chase. Further incubation in fresh medium containing unlabeled uridine resulted in complete cessation of incorporation of label into acid-insoluble material. At the end of the 80-min chase period at least 50% of the label in the acid-soluble pool was present as UTP, regardless of uridine concentration or whether or not unlabeled uridine was present during the chase period. In cells resuspended in labeled uridine, the amount of label in both total cell material and acid-insoluble material began to increase immediately after re-addition of label to pulse-chased cells and the rates of incorporation were approximately the same as during the pulse-labeling period. Thus, the added uridine appeared to enter RNA without passing through the pool of UTP accumulated during the initial labeling period. Substitution of adenosine for uridine resulted in similar findings but thymidine seemed to be incorporated through a single pool.

- 2545 MICROBODIES OF MORRIS HEPATOMAS. (E.) Mochizuki, Y. (Dept. Path., U. Chicago, Ill.), Z. Hruban, H. P. Morris, A. Slesers and J. Vigil. *Cancer Res* 31 (6):763-773, 1971.

Thirty-six varieties of Morris hepatomas were examined for the presence of microbodies and for activity of 3 microbody enzymes: catalase, urate oxidase and D-amino acid oxidase. The hepatomas from rats were either fast-growing, slow-growing or of intermediate growth rate. Microbodies were present in all hepatomas examined except for hepatomas 3683 (fast-growing), 7794A (intermediate) and BRL-4-C-3 (slow-growing). Microbodies were seen as round or ovoid particles limited by a membrane; they were always in contact with smooth portions of rough cisternae and sometimes with tubular endoplasmic reticulum and lipid droplets. Microbodies were relatively rare in fast-growing hepatomas, and those which were seen in fast-growing tumors were comparatively small (0.2-0.4 μ). Crystalloids were also rare in fast-growing hepatomas. In intermediate growth rate hepatomas, microbodies were more abundant and larger (0.4-1.0 μ), and crystalloids were common. Slow-growing hepatomas contained microbodies with frequency comparable to or exceeding the frequency with which microbodies were found in intermediate-rate tumors. These microbodies were larger than those found in intermediate-rate tumors (0.2-1.3 μ); crystalloids were seen in slow-growing tumors with about the frequency with which they were seen in intermediate-rate tumors. Hepatomas with numerous large microbodies (e.g., slow-growing and intermediate growth rate tumors) usually had high catalase and D-amino acid oxidase activity levels (e.g., 50-100 U catalase/mg protein and 40-80 U D-amino acid oxidase/mg protein). Hepatomas with scarce or small microbodies (e.g., fast-growing tumors) usually had relatively low values for catalase and D-amino acid oxidase activity (e.g., 3-12 U catalase/mg protein and 0-7 U D-amino acid oxidase/mg protein).

protein). Hepatomas with high urate oxidase activity usually had large crystalloids in the bodies. Urate oxidase and D-amino acid oxidase activities did not correlate with hepatoma growth rate.

DIFFERENCE OF RNA POPULATION BETWEEN NORMAL LIVER AND HEPATOMA AH-130. (E.) Ono, T. (Cancer Inst., Tokyo, Japan), M. Kawamura, M. Hyodo and K. Wakabayashi. *Gann* 62(1):31-40, 1971.

In a rapidly growing rat ascites hepatoma designated AH-130 was compared with RNA in normal rat liver using RNA-DNA hybridization techniques in order to determine the hybridization efficiency of hepatoma RNA compared with that of normal liver. Competition experiments revealed that the hepatoma lacked a fraction of liver cell RNA present in normal liver and that tumor cell liver RNA synthesized a fraction not found in normal liver. These results were obtained using whole cell RNA in the competition experiments; when nuclear RNA was used it was found that a fraction of liver cell RNA present in normal cells was missing from hepatoma RNA, but no RNA fractions present in hepatoma RNA were absent from normal cell RNA.

ENZYME PATTERNS IN A GROUP TRANSPLANTABLE MOUSE HEPATOMAS OF DIFFERENT GROWTH RATES. (E.) Bresnick, E. (Dept. Pharmac., Baylor Coll. of Medicine, Houston, Texas), E. D. Mayfield, Jr., A. G. S. and R. A. Liebelt. *Cancer Res* 31(7):743-751, 1971.

Hybrid mice were given s.c. implantations of 1-2 fragments of viable spontaneous, methylcholanthrene-induced hepatoma tissue and the resulting tumor tissue was assayed for enzyme activity. The time from inoculation until the tumor reached approximately 1 cm in diameter ranged from 30-60 days for the first transplant generation. Subsequent transplantation generations revealed a progressive decrease in growth period. The morphological pattern in general remained stable compared to the primary tumor structure in all except 2 hepatomas. Distribution of glycogen was similar to that of normal liver in approximately half of the hepatoma lines in the first transplant generation; however, 5 hepatomas were free of histochemically demonstrable glycogen following subsequent transplantation. Cytoplasmic inclusion bodies, present in primary tumors, were absent in transplants. Glutamate transcarbamylase was elevated in all but one hepatoma while ornithine transcarbamylase decreased in all hepatomas; carbamylphosphate synthetase revealed 10% of the activity found in normal liver in only 1 hepatoma. Uracil reductase activity was less than 10% of normal in all hepatomas, except in 2 hepatomas which revealed 25% and 50% activity. The individuality of enzymic complement could be an expression of genetic origin or of manner of induction of the neoplasm.

2548 CHOLESTEROL BIOSYNTHESIS IN TRANSPLANTABLE HEPATOMAS: EVIDENCE FOR IMPAIRMENT OF UPTAKE AND STORAGE OF DIETARY CHOLESTEROL. (E.) Harry, D. S. (Royal Free Hosp., London, England), H. P. Morris and N. McIntyre. *J Lipid Res* 12(3):313-317, 1971.

Rats bearing transplanted Morris hepatomas (numbers 7793, 7794A and 7787) were fed a diet containing 2% cholesterol for periods of up to 21 days, and cholesterol biosynthesis was observed in tumor-bearing and tumor-free rats on the cholesterol-rich diet. Incorporation of acetate into cholesterol was inhibited by cholesterol feeding, but acetate incorporation was unaffected in tumor tissue. Livers of cholesterol-fed rats accumulated large amounts of cholesterol esters; however, the hepatomas showed little or no increase in cholesterol ester content. When tritium-labeled cholesterol-1 α was administered intragastrically to tumor-bearing rats it was found that the uptake of ^3H by tumors was slower than uptake of ^3H by normal livers. Apparently, the insensitivity of cholesterol biosynthesis to dietary cholesterol in Morris hepatomas was due to impaired incorporation and storage of dietary cholesterol.

2549 SURVEY OF SOME ENZYME PATTERNS IN TRANSPLANTABLE REUBER MOUSE HEPATOMAS. (E.) Reynolds, R. D. (McArdle Lab., U. Wisconsin Med. Ctr., Madison), V. R. Potter, H. C. Pitot and M. D. Reuber. *Cancer Res* 31(6):808-812, 1971.

Spontaneously arising hepatomas in C3H x Y hybrid mice were transplanted s.c. bilaterally into the hind legs of 4-7-wk-old C3H x Y mice and were then used for enzyme pattern surveys. Tyrosine aminotransferase, serine dehydratase and citrate cleavage enzyme generally showed lower values in host liver; however, tyrosine aminotransferase levels rose in response to a high-protein diet in 4 hosts with hepatomas. Glucose-6-phosphate dehydrogenase showed similar values in all host livers and hepatomas studied. The results obtained resemble those obtained from a series of diploid Morris hepatomas.

2550 DISTINCTIVE PROPERTIES OF FERRITIN FROM THE REUBER H-35 RAT HEPATOMA. (E.) Lee, J. C. K. (U. Rochester Med. Ctr., N. Y.) and G. W. Richter. *Cancer Res* 31(5):566-572, 1971.

S.C. hepatoma transplants grown in female weanling ACI rats loaded with iron were pooled, analyzed and compared with normal rat liver by means of electrophoresis and spectrophotometric analysis. The proportions of ferritin obtained from H-35 hepatomas were 90.2% α (monomer), 8.9% β (dimer), and 0.9% γ (trimer), compared to ferritin from ACI rat liver which contained 80.9% α (monomer), 13.7% β (dimer), and 5.3% γ (trimer). The isoelectric point of H-35 ferritin, pH 4.95 ± 0.03 , was significantly lower than that of ACI rat liver ferritin, pH 5.20 ± 0.02 . The ratios of ferritin monomers from H-35 tumors to ferritin from ACI rat livers in the pH 5.5 eluate

from an ion exchange column was higher than at pH 7.2. Quantitative amino acid analysis revealed significant differences in all but aspartic acid, glycine and phenylalanine content. Ultracentrifugation gave a sedimentation coefficient for ACI rat liver apoferritin of 17.80S and for H-35 hepatoma of 17.94S. Both kinds of ferritin produced a plateau of maximal absorption between 230 and 280 nm, and above 280 nm the absorbance slowly declined. Crystal formation revealed similar octahedral structures in both ferritins; these structures were indistinguishable from each other when examined by electron microscopy.

- 2551 TURNOVER OF TYROSINE TRANSAMINASE IN CULTURED HEPATOMA CELLS AFTER INHIBITION OF PROTEIN SYNTHESIS. (E.) Barker, K. L. (Oak Ridge Natl. Lab., Tennessee) K. L. Lee and F. T. Kenney. *Biochem Biophys Res Commun* 43(5):1132-1138, 1971.

Hydrocortisone-induced monolayer cell cultures of the Reuber (H-35) hepatoma were treated with cycloheximide or puromycin to study the dynamics of tyrosine transaminase turnover. Addition of 5 µg/ml of cycloheximide to H-35 cells maximally induced with 5×10^{-7} mole of hydrocortisone led to a decline in enzyme levels during the first hr, when the half-life of the enzyme became 1.6 hr. The rate of enzyme inactivation decreased thereafter, so that its half-life became about 10 hr between 4 and 9 hr after addition of the inhibitor. The cells were functionally viable after 3 hr treatment with cycloheximide. The levels of tyrosine transaminase increased to 96% of those present in maximally induced uninhibited cells 1 hr after removal of the inhibitor. The cells retained their capacity both to inactivate tyrosine transaminase and to have the synthesis of this enzyme reinduced by hydrocortisone. Tyrosine transaminase turnover was blocked between 4 and 6 hr after addition of puromycin. The reversibility of the cycloheximide effect on tyrosine transaminase suggests that no generalized toxic effects occurred in the cultured cells.

- 2552 INFLUENCE OF SPLENECTOMY ON THE DEVELOPMENT OF LEUKEMIA IN MALE MICE OF THE ICRC STRAIN. (E.) Pai, S. R. (Cancer Res. Inst., Tata Memorial Centre, Parel, Bombay 12, India) and K. J. Ranadive. *Life Sci* 10(8):475-479, 1971.

Twenty randomly selected weanling male mice of the ICRC strain were subjected to splenectomy in order to investigate the role of the spleen in the development of spontaneous leukemia. Another group of intact males were given a previous i.p. injection of leukemic spleen homogenate and were subjected to splenectomy when palpable tumors developed. One of 20 intact control mice developed a generalized lymphocytic leukemia at 14.5 months, and 3 out of 20 splenectomized males developed lymphosarcoma at 9, 11 and 13 months. None of the splenectomized animals developed leukemia following transplant of leukemic spleen cells, while 6 out of 6 intact litter-mate controls given leukemic spleen cells

developed leukemia. Splenectomy after the development of palpable tumors had no prophylactic effect on the hosts since all the animals receiving transplants died 1 wk after the operation. Removal of the spleen did not reduce the incidence of leukemia under the given experimental conditions, which indicates that organs other than the spleen are involved in the development of leukemia.

- 2553 GLUCOSE AND ACETATE UTILIZATION BY HYPERPLASTIC, ALVEOLAR NODULE OUTGROWTHS FROM ADENOCARCINOMAS OF MOUSE MAMMARY GLAND. (E.) Bartley, J. C. (Children's Hosp. Med. Ctr. No. 1, California, Oakland), H. McGrath and S. Abraham. *Cancer Res* 31(5):527-537, 1971.

Mammary tissue from normal lactating C3H mice, pregnant and lactating mice with mammary adenocarcinoma, and from mice with hyperplastic alveolar nodules was studied for the utilization of radioactive glucose-1-¹⁴C, glucose-6-¹⁴C, -6³H, and 1-¹⁴C. Lactate production, CO₂ production, 1-¹⁴C and pentose phosphate cycle activity were also measured. Normal lactating mammary glands showed the highest metabolic activity in all parameters except lactate production; tumor tissue exhibited the lowest metabolic activity. The values of the various parameters for hyperplastic alveolar nodule tissues were intermediate to values recorded for normal tissue from suckled mice. The addition of glucose to tissue preparations stimulated the incorporation of glucose into fatty acids; glucose stimulation was not marked in tumor tissue as in normal mammary tissue. Glucose and acetate utilization by normal mammary tissue from pregnant mice was similar to that of hyperplastic alveolar nodule tissue, and the utilization of glucose and acetate in tumor tissue was minimal.

- 2554 THE ANALYSIS OF MALIGNANCY BY CELL HYBRIDS BETWEEN TUMOUR CELLS AND NORMAL CELLS. I. HYBRIDS BETWEEN TUMOUR CELLS AND NORMAL CELLS. DERIVATIVES. (E.) Klein, G. (Dept. Tumour Biology, Karolinska Inst., Stockholm, Sweden), U. Bregander, F. Wiener and H. Harris. *J Cell Sci* 8(3) 659-671, 1971.

Hybrids were produced by fusing normal L cells with the A9, B82 or A9RI cell line with tumor cell lines, and the growth of these cell hybrids was examined by inoculating them in syngeneic hosts. Tumor cells used in the fusion production of hybrids included an Ehrlich tumor derived from a mouse, 2 ascites sarcomas (SEWA and SEWA-2) and 2 lymphomas (YAC and YACIR). Ehrlich/A9 hybrids contained the marker chromosomes peculiar to each of the parent lines, and had a modal number of 128 chromosomes. They had a low level of tumorigenicity in irradiated newborn mice, indicating the high malignancy of the Ehrlich tumor cells was not transmitted to its hybrid. Cells from the hybrids which did ensue after inoculation of syngeneic hosts with the Ehrlich/A9 tumor cells had a lower chromosome number than did the hybrid cells which contained marker chromosomes of both hybrid

rid cells produced by fusing A9 cells with cells from the other tumors had modal chromosome numbers approximately equaling the sum of the modal numbers of each parent cell. In all cases, the malignancy of the tumor cells was modified by fusion with the other cells; the hybrids had a low malignancy compared with that of the parent tumor cell. Chromosome numbers in hybrid tumor cells were lower in all cases than in the hybrids. B82 cells also appeared to suppress the malignancy of Ehrlich tumor cells in hybrids of the 2 cells. When Ehrlich cells were fused with A9RI cells, the malignancy of the hybrid was again found to be slight compared to that of the Ehrlich cell parent. When Ehrlich/A9 hybrid cells were grown *in vitro* for 18 months (a period judged sufficiently long for some general chromosome loss to occur) prior to inoculation into mice, the malignancy of the hybrid cells was not markedly enhanced, suggesting that the loss of a *specific* chromosome (other than a general reduction in number) is required for hybrid cells to grow *in vivo*.

5 A SPONTANEOUS MESENCHYMAL CELL NEOPLASM IN THE ADULT NEWT, *DIEMICTYLUS VIRIDESCENS*.

Burns, E. R. (Dept. Anat., U. Arkansas Med. C., Little Rock) and H. J. White. *Cancer Res* 31(5):826-829, 1971.

Tumor mass was seen protruding from the left side of an American newt (*Diemictylus viridescens*); the tumor had been collected in an unpolluted fresh water pond and had not been deliberately inbred. Multiple parastitic inflammatory lesions are not uncommon in the order Urodela, cancerous lesions are rare. On light microscopy, the tumor was found to be composed of epidermal and muscle cells, and had invaded skeletal muscle tissue. Tumor cells showed varying degrees of nuclear and cytoplasmic pleomorphism; cells contained large hyperchromatic and pycnotic nuclei and occasionally had prominent nucleoli. No extensive necrosis was seen in the tumor and no mitotic figures were present; PAS-positive granules were seen in the cytoplasm of tumor cells. The lesion was described as mesenchymal cell neoplasm.

6 PLASMA RENIN ACTIVITY IN WILM'S TUMOUR.

(E.) Voute, P. A., Jr. (Emma Child. Hosp., Amsterdam, Netherlands), J. van der Meer and W. Gaard-Kloosterziel. *Acta Endocr* 67(1):197-202, 1971.

Plasma renin activity (PRA) was assayed in 8 children with Wilm's tumor, both before and after nephrectomy in 5 of the cases. The patients ranged in age from 1 yr and 8 months to almost 4 yr, and 6 males and 2 were females. Five of the patients had tumor metastases. The level of PRA was lower in all children than in children with Wilm's tumor before nephrectomy; PRA for normals range from 35-100 ng/10 ml/3 hr, compared to PRA for Wilm's tumor patients prior to nephrectomy which range from 150-1000 ng/10 ml/3 hr. Post-nephrectomy values for PRA in the Wilm's tumor group were similar to those seen in normal children.

2557 SOME BIOCHEMICAL AND CYTOGENETIC PROPERTIES OF RAT THYROID TUMORS. (E.) Wu, C. (Dept. Biol. Chem., U. Michigan, Ann Arbor), A. A. Al-Saadi, R. C. Ling and K. L. McKinnie. *Cancer Res* 31(5):577-582, 1971.

Tumors produced by s.c. transplantation of the goiters of rats fed a Remington low-iodine diet for 12-16 months into the flanks of thyroidectomized Fischer rats and then into intact rats were subjected to biochemical and cytogenetic studies. Three of the 4 transitional tumors studied were well-differentiated adenomas and 1 was moderately to poorly differentiated. All 4 tumors had a modal chromosome number of 42 in 63-84% of the cells; the percentage of aneuploidy ranged from 16-36% with 10% or more of the cells having 41 chromosomes. The 4 autonomous tumors studied were all undifferentiated, fast-growing, metastasizing carcinomas. All autonomous tumors had numerically and/or structurally altered karyotypes in 100% of their cells. Most of the cells of autonomous tumors were characterized by the loss of 1 chromosome of Pair 15; the dropping of this chromosome may be associated with the progression of the tumor from the transitional to the autonomous stage. The uptake of ^{131}I by the thyroid of tumor-bearing animals was lower than the uptake by normal thyroid; no difference in uptake was observed between rats bearing autonomous or transitional tumors. The uptake of ^{131}I by the tumors was about 1/15th that of the total uptake of the host thyroid; the labeled iodine entering the tumor appeared not to be incorporated into organic compounds. The activity of iodide peroxidase was decreased in the thyroid of animals bearing thyroid tumors (transitional or autonomous). The transitional tumors showed a level of enzyme activity intermediate between that of normal and host thyroid. No measurable peroxidase activity was found in any of the autonomous tumors.

2558 ELECTRON MICROSCOPIC OBSERVATIONS ON STRUCTURES RESEMBLING MYXOVIRUS IN HUMAN SARCOMAS. (E.) Györkey, F. (VA Hosp., Houston, Texas), J. G. Sinkovics and P. Györkey. *Cancer* 27(6):1449-1454, 1971.

Cytoplasmic structures resembling strands of paramyxovirus ribonucleoprotein were observed under the electron microscope in preparations of human tumors of mesenchymal origin; tumor material included biopsies of rhabdomyosarcomas, liposarcomas, chondrosarcomas, osteosarcomas, fibrosarcomas, neurofibrosarcomas and Kaposi's sarcoma, and primary tissue cultures of rhabdomyosarcomas, chondrosarcomas, fibrosarcomas and osteosarcomas. All rhabdomyosarcomas and some liposarcomas, osteosarcomas, fibrosarcomas and Kaposi's sarcomas contained filamentous and tubular cytoplasmic structures. Structures were found in tissue cultures as well as in biopsy material. The filamentous and tubular structures were located in the cytoplasm in aggregates of varying sizes; in some cases the aggregates were membrane-bound. In Kaposi's sarcoma, the structures were found between nuclear membranes. The filaments measured 200-220 Å in diameter and up to 1000 Å in length. Fila-

ments in cross section were sometimes electron-dense and sometimes lucent. The nature and function of these structures is unknown.

- 2559 MELANOTIC AND AMELANOTIC MELANOMAS IN XIPHOPHORIN FISH. (E.) Vielkind, J. (Genet. Inst., Justus Liebig-U. Giessen, German), U. Vielkind and P. Anders. *Cancer Res* 31(6): 868-875, 1971.

Preparations of inherited melanotic and albino melanomas carried by hybrids of the platyfish and swordtail species of xiphophorus fish were examined under the electron microscope; among both pigmented and albino melanomas, a rapidly growing form and a more slowly growing form were examined. Rapidly growing melanotic melanomas were found to consist of melanocytes only, which were slightly dendritic or spindle-shaped and contained ovoid nuclei. Rapidly growing albino melanoma cells were relatively anaplastic, but otherwise resembled rapidly growing melanotic melanoma cells; however, in the albino cells there were only a few premelanosomes in the cytoplasm, while in melanotic melanomas the cytoplasm contained abundant premelanosomes. Slowly growing melanotic melanomas of some albino hybrids consisted of large dendritic melanocytes. Albino melanomas were found to possess a higher DNA content/U fresh weight than melanotic melanomas. The albino melanomas appeared to be more malignant than the melanotic melanomas.

- 2560 RECENT ADVANCES IN THE ULTRASTRUCTURE OF MALIGNANT MELANOMA. (E.) Cesarini, J. P. (Regional Anti-Cancer Ctr., Marseille, France). *Rev Europ Etud Clin Biol* 16(4):316-322, 1971.

Melanocytes from benign and malignant melanomas were examined under the electron microscope. No alteration of the maturation of the melanosomes within the melanocytes or of the deposition of pigment was seen in benign tumors, and the protein in the melanocytes remained regular. The protein structure of melanocytes in pigmented malignant melanomas was disorganized, folded and broken; the deposition of melanin on the protein was irregular. The maturation of the melanosomes was disrupted in malignant cells. In the Dubreuilh-Hutchinson melanosis which affects elderly women, an increase in melanocytes at the expense of keratinocytes was seen to mark the onset of a precancerous condition. Ultrastructural examination of amelanotic melanoma melanocytes showed 2 cell types: one type of cell contained premelanosomes which did not develop into mature melanosomes, and the other contained no premelanosomes.

- 2561 DNA POLYMERASES FROM HUMAN CELLS. (E.) Weissbach, A. (Roche Inst. Molec. Biol., Nutley, N. J.), A. Schlabach, B. Fridlender and A. Bolden. *Nature* 231(23):167-170, 1971.

Two DNA polymerase activities have been isolated from the nucleus of HeLa cells and in the normal

human lung diploid line WI-38. One of the DNA polymerase activities (I) was found only in the nucleus in normal conditions, and the other (II) resembled the single DNA polymerase activity found in the cytoplasm. The HeLa cell cytoplasmic and nuclear enzyme II showed an optimal response with 5-10 mM Mg^{2+} , whereas nuclear enzyme I approached maximum activity at 15-26 mM Mg^{2+} . All 3 DNA polymerases were inhibited by high salt concentrations. *p*-Chloromercuribenzoate (25 μ M) did not affect nuclear enzyme I, but inhibited nuclear enzyme II and the cytoplasmic enzyme almost completely. Nuclear enzyme I was 2-3 times more sensitive to inactivation in the presence of 200 μ g/ml of bovine serum albumin at 45°C than the other DNA polymerases. DNase I-treated double stranded DNA was an effective primer for the HeLa DNA polymerase. The dependence of the reaction on all 4 deoxyribonucleoside triphosphates was established. Mycoplasma and other contaminating organisms were not detected in the HeLa cell cultures from which the DNA polymerases were isolated.

- 2562 "BENIGN METASTASIZING GOITER" OF CONGENITAL ORIGIN: AN EXPERIMENTAL STUDY WITH THE TRANSPLANTABLE THYROID TUMOR OF THE RAT. (E.) Matvinov, J. (U. Michigan Sch. Med., Ann Arbor), R. H. Nishiyama, A. Lalli and G. Poissant. *Cancer Res* 31(2):288-296, 1971.

Male rats were given injections of 100,000 cells from a papillary-follicular thyroid tumor containing apparently normal follicles; rats were injected into the heart, jugular or mesenteric vein, medullary canal of the femur, or subcutaneously. All animals developed tumor implants following injection of tumor cells; rats injected in the heart developed 40 lung tumor implants and 4-5 liver tumor implants. Tumors developed more rarely in spleen, kidney, and vertebrae. Some tumor implants consisted of normal-appearing follicles in lungs, kidneys, spleen, or vertebrae and were virtually indistinguishable from implants of normal thyroid tissue in the same organs. Injection of tumor cells in the heart produced tumor implants in all lobes of the liver which appeared as papillary tissues and normal-appearing follicles. Papillary and papillary-follicular implants were seen in muscle which did not contain normal-appearing follicles. Implants similar to the parent tumor were seen in the medullary canal of the femur and in the skin. Iodine metabolism was studied in the implants by observing the concentrations of ^{131}I injected into rats with tumor cell implants. The ^{131}I uptake of the thyroid gland in tumor-bearing rats was lower than in rats without tumors; the protein-bound iodine in tumor-bearing rats (5.0-100 μ g/ml) was higher than that in tumor-free rats (1.0-100 μ g/ml). The ^{131}I uptake by s.c. implants was higher than the uptake by the thyroid gland; however, the tissue of the implants was 26 times as active on a per unit wt basis than the thyroid tissue samples dissected from tumor implants from the same rats. Tumor implants in the thyroid and other internal organs concentrated about 4 times more ^{131}I than similar samples from s.c. tumor implants. The concentration of ^{131}I was highest in the normal-appearing lung follicles. The differentiation

Baylor Coll. Med., Houston, Texas), H. J. Spjut,
M. N. Smith and F. Rapp. *Cancer* 27(6):1440-1448,
1971.

3):361-366, 1971.

Electron microscopic examination of cells prepared from an osteoblastic osteosarcoma developed in the right humerus of a 15-yr-old male revealed branched tubular intracytoplasmic structures in primary tumor cells and in lung metastases. Tubular structures were seen in tumor cells, endothelial cells and lymphocytes and were localized in the endoplasmic reticulum. These tubular structures had 2 distinct patterns: in one pattern, the cisternae of the endoplasmic reticulum were dilated and the tubules had a uniform diameter; and in the other pattern, the endoplasmic reticulum surrounded the tubules tightly and the latter had a sieve-like appearance. The tubules appeared to have originated by the development of particles condensed from the endoplasmic reticulum. The tubular structures measured 20-31 μ m in diameter, and had a core containing fine granules. Although it was suggested that the tubules might be measles virus nucleocapsids, this hypothesis was rejected on the basis of morphological differences between the osteosarcoma tubules and measles virus nucleocapsids.

SE OF THE DISEASE. (Ger.) Müller, D. (Med. Col. Clin., Tübingen, Germany). *Acta Histochem* (pl. 9):201-206, 1971.

2566 MULTIPLE PRIMARY TUMORS INCLUDING BILATERAL BREAST CANCERS IN A MAN WITH KLINEFELTER'S SYNDROME. (E.) Coley, G. M. (Dept. Surg., Hartford Hosp., Hartford, Conn.), R. D. Otis and W. E. Clark II. *Cancer* 27(6):1476-1481, 1971.

A case report is described in which a 34-yr-old man with Klinefelter's syndrome developed, over a period of 20 yr, 6 separate primary tumors, including chondroma of the sacrum, lipoma on the back chest wall, spongioblastoma of the brain, carcinoma of the breast (Paget's disease), papillary carcinoma and cervical metastases of the thyroid, and a second Paget's carcinoma of the breast. The intervals between diagnosis of the several tumors range from 0.5-8 yr. Although associations have been reported between Klinefelter's syndrome and breast cancer, the present case was thought to be unique in view of the number of separate primary tumors. The experience of multiple tumors, especially of the breast, which occur with increased frequency in men with Klinefelter's syndrome suggests both genetic and hormonal factors are involved in the etiology of the tumors.

(E.) Nathanson, L. (Dept. Med., New England Med. Ctr., Boston, Mass.) and W. Fishman. *Cancer* 27(6):1388-1397, 1971.

Sera from 323 patients with malignancy confirmed by histologic examination was quantitated for the presence of Regan phosphatase isoenzyme. A positive identification of Reagan isoenzyme was made in 12% (39) of the patients; those suffering from ovarian and pancreatic carcinoma had the highest incidence

7-JUNE 1971

of the isoenzyme, followed by gastric, breast, and lung cancers and the sarcomas. The majority of patients who were Regan negative had a heat-stable alkaline phosphatase of less than 0.8 U. In a group of cancer patients with elevated phosphatase, an almost 3-fold greater incidence of Regan isoenzyme was observed than in the group of cancer patients unselected for hyperphosphatasemia. In addition, persons with hepatic and intestinal disease of a non-malignant nature were found to be positive for the presence of Regan isoenzyme. The biological significance of this isoenzyme seems to lie in its role as an additional carcinoembryonic system.

- 2568 ULTRASTRUCTURE OF GRANULAR CELL AMELOBLASTOMA. (E.) Navarrette, A. R. (Baylor Coll. Med., Houston, Tex.) and M. Smith. *Cancer* 27(4):948-955, 1971.

An electron microscopic study was performed on tumor tissue from a granular cell ameloblastoma developing on the jaw of a 47-yr-old Negro woman. Under the light microscope, the tumor was seen to be composed of numerous neoplastic epithelial islands in a scant, mature fibrous stroma. In the centers of the islands were large eosinophilic granular cells of varying shapes containing cytoplasmic granules of varying sizes. The granules were PAS-positive. On electron microscopic examination, tumor cells were seen to have numerous lysosome-like pleomorphic osmiophilic granules in the cytoplasm. Granules had different structures; some showed concentrically laminated membranes and others were composed of bundles of fine parallel membranes running in different directions. Large round degenerative cytoplasmic masses were also seen. In addition to the granules, cytoplasm contained round or oval mitochondria, well developed Golgi complexes and scant rough-surfaced endoplasmic reticulum. The cytoplasmic granules in the ameloblastoma resembled those seen in the granular cell myoblastoma.

- 2569 GASTRIC POLYPS: HISTOLOGIC TYPES AND THEIR RELATIONSHIP TO GASTRIC CARCINOMA. (E.) Tomasulo, J. (Dept. Path., Hosp. U. Pennsylvania, Philadelphia). *Cancer* 27(6):1346-1355, 1971.

Case histories of 97 patients with gastric polyps were studied with the result that 35% of the polyps were found to have occurred in stomachs of patients with gastric carcinoma. Neither singly occurring polyps, multiple discrete polyps nor gastric polyposis was correlated with carcinoma to a higher degree than the other polyp conditions. Hyperplastic polyps were more common than adenomatous polyps, the former accounting for 76% of cases. Hyperplastic polyps were randomly distributed throughout the stomach, while adenomatous polyps were usually located antrally and were similar to colonic polyps. Only in association with adenomatous polyps was *in situ* carcinoma seen. Fifty-nine percent of adenomatous polyps and 28% of hyperplastic polyps were associated with carcinoma.

- 2570 RIBONUCLEOPROTEIN PARTICLES INVOLVED IN HeLa MITOCHONDRIAL PROTEIN SYNTHESIS. (E.) Brega, A. (Massachusetts Inst. Tech., Cambridge) and C. Vesco. *Nature* 229(5):136-139, 1971.

The relation between ribonucleoprotein particles and protein synthesis in HeLa cell mitochondria was investigated according to functional criteria by selective labeling in the presence of suitable inhibitors. A sucrose gradient analysis of mitochondrial structures carrying nascent peptide chains after pulse-labeling of cells in the presence of pederine (which inhibits cytoplasmic protein synthesis) showed most of the incorporated radioactivity to be associated with structures of 180S or greater except for 1 small peak in the 40S position. Chloramphenicol and pederine together blocked label incorporation into both the 55S and 40S larger structures. The radioactivity of the 55S region of the sample treated with pederine disappeared during 5 min of incubation with puromycin, confirming that the label had been incorporated into nascent peptide chains. Most of the protein synthesizing structures were sensitive to antibiotics and sedimented faster than 55S, whereas most of the ethidium bromide-sensitive RNA sedimented more slowly and the 40S peak seemed to be rather unsymmetrical. Monomers and subunits were subjected to further gradient centrifugation analysis; the data obtained from these experiments suggest that 21S and 12S RNA comprise a set of ribonucleoprotein particles qualitatively similar to those already described in *Xenopus* (12S, a ribosome smaller than the cytoplasmic ribosome, composed of 2 ribosomal subunits). The 55S ribonucleoprotein particle appears to be the mitochondrial monosome, while the heavy structures the mitochondrial polyribosomes.

- 2571 FACTORS STIMULATING CELL GROWTH COMPARED BY ISOELECTRIC FOCUSING. (E.) Ecsenyi, M. (St. Bact. Lab., Stockholm, Sweden). *Exp Cell Res* 65(1):123-128, 1971.

Growth stimulating factors were extracted from human and leukemic urine, serum from patients with acute lymphomas and normal plasma. The growth stimulating capacities of these factors were studied by isoelectric focusing. A purified fraction of normal human serum showed a stimulatory effect on growth of human marrow cells. The active substances of the different materials were compared by determining the isoelectric points. All the growth factors focused at pH 4.05-4.06. The stimulating factor prepared from a medium containing embryonic mouse cells gave a lower isoelectric point than the human material, focusing at pH 3.92-3.93.

- 2572 NUCLEOTIDE POOLS OF NOVIKOFF RAT HEPATOMA CELLS GROWING IN SUSPENSION CULTURE: KINETICS OF INCORPORATION OF NUCLEOSIDES INTO NUCLEOTIDE POOLS AND POOL SIZES DURING GROWTH. (E.) Plagemann, P. G. W. (Med. Sch. U. Minnesota, Minneapolis). *J Cell Physiol* 77(2):213-240, 1971.

Novikoff rat hepatoma cells (subline N1S1-67) which had been incubated with tritium-labeled uridine, adenosine or thymidine were used to prepare RNA

hydrolysates which were chromatographically and electrophoretically examined. Subsequent to incubation with ^{14}C -4-aspartic acid, 80-90% of the radioactivity was found in RNA and the remainder was present in DNA; half of the label was found in CMP and half in GMP. The presence of uridine almost completely inhibited the incorporation of aspartic acid into nucleic acids found in alkali hydrolysates with no inhibition of label into the acid-soluble fraction was seen. Incorporation of uridine at all concentrations proceeded 6-7 times more rapidly into the acid-soluble nucleotide pool than into the acid-insoluble material, and maximum velocity was approached at 100 μM uridine in the medium. Similar results were reported for adenosine uptake, except that saturation of the transport reaction occurred at 10 μM and simple diffusion became the predominant mode of entry above 100 μM . At 200 μM , incorporation of either uridine or adenosine into total cell material followed a biphasic pattern; approximately constant rates were established for 10 min with uridine and for 120 min with adenosine followed by a rapid increase of 70-80% before a second constant level was attained.

73 THE GERMINATIVE TUMOURS OF TESTICLES. (Ger.) Schaudig, G. (Clin. Radiat. Ther., Roentgenol., U. Marburg/Lahn, Germany), L. Buchelt and F. H. Strahlentherapie 141(5):495-507, 1971.

74 CYTOGENETIC STUDIES AT VARIOUS STAGES OF DEVELOPMENT BY CHRONIC MYELOLEUKEMIA. (Rus.) Krennevskaya, M. I. (Central Inst. Hematol. Transfusion, Min. Pub. Hlth., Moscow, U.S.S.R.), T. P. Nevskaya, T. A. Cherntsova and E. I. Terentjeva. Probl. Genet 16(2):23-29, 1971.

75 ON MALIGNANT TRANSFORMATION OF ECCRINE SPIRADENOMA. (Pol.) Dabska, M. (Z. Zakladu Onkol., Nowotworow Inst. Oncol., Warsaw, Poland). Nowotwory 21(1):37-45, 1971.

76 FAMILIAL LEUKAEMIA OR A NEW SYNDROME? (Pol.) Nowakowski, T. K. (Z. I. Clin. Radiat., Wroclaw, Poland), M. Zawartka, R. Kowalski, J. Pellar and J. Wartenberg. Pediat Pol 46(4):495-502, 1971.

77 CHROMOSOME ABNORMALITIES IN A CASE OF ACUTE HISTIOLEUKAEMIA. (It.) Bersi, M. (Med. Hosp., Verbania Hosp., Novara, Italy), C. Gasparini and G. Cardini. Minerva Med 62(21):1120-1124, 1971.

78 LEUKAEMIA AND CARCINOMA. (Ger.) Werner, W. (Path. Inst., Humboldt-U. Berlin, Germany), A. Khalatbari. Arch Geschwulstforsch 37(1):9-18, 1971.

2579 SOME CHARACTERISTICS OF NEWLY SYNTHESIZED DNA FRACTIONS FROM MAMMALIAN CELLS ELUTABLE FROM METHYLATED ALBUMIN KIESELGUHR COLUMNS BY NaCl . (Ger.) Probst, H. (Physiol. Chem. Inst., U. Tübingen, Germany). Hoppe Seyler Z Physiol Chem 352(5):748-756, 1971.

2580 STUDY OF THE MORPHOLOGY AND SECRETION OF AN EXPERIMENTAL CORTICOTROPHIC TUMOR IN THE RAT. (Fr.) Pelletier, G. (Albert Einstein Coll. Med., Bronx, N.Y.), F. Peillon, M. T. Pham Hun Trung and J. Racadot. Rev Europ Etud Clin Biol 16(1):79-83, 1971.

2581 SIPPLE'S SYNDROME (PHEOCHROMOCYTOMA AND THYROID CARCINOMA) WITH BILATERAL BREAST CARCINOMA. (E.) Lima, J. B. (Dept. Surg., Kaiser Fdn. Hosp., San Francisco, Calif.) and P. D. Smith. Am J Surg 121:732-735, 1971.

2582 SMOLDERING ACUTE LEUKEMIA: CLINICAL AND CYTOGENETIC STUDIES IN SIX PATIENTS. (E.) Knospe, W. H. (Rush Presbyterian-St. Luke's Med. Ctr., Chicago, Ill.) and S. A. Gregory. Arch Intern Med 127(5):910-915, 1971.

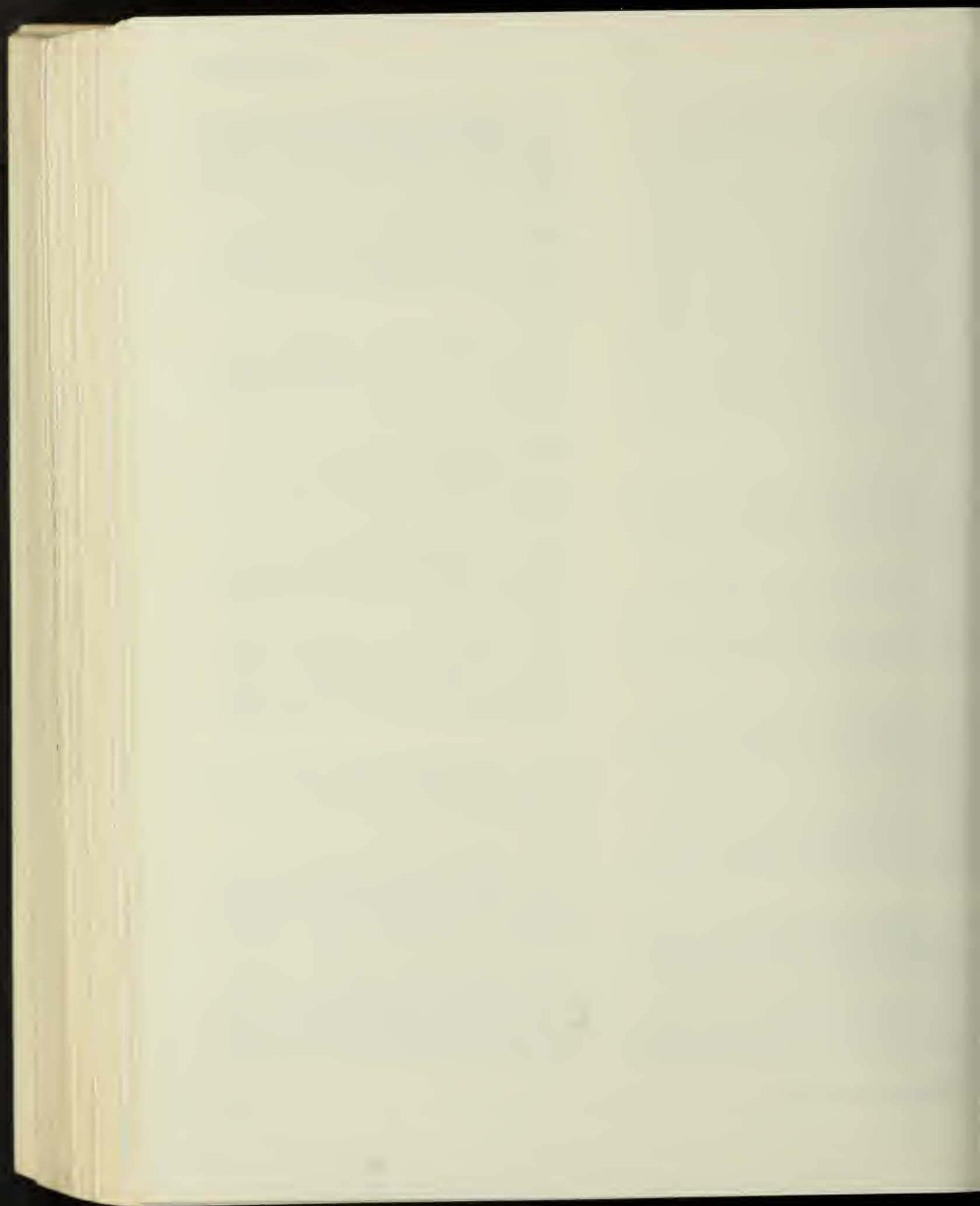
2583 PHACOMATOSES, THE INHERITANCE OF CANCER, AND SOMATIC MUTATION. (E.) Nicholls, E. M. (Sch. Human Genet., U. New South Wales, Australia). Clin Genet 1(5-6):245-257, 1970.

2584 DNA SYNTHESIS IN CIRCULATING LYMPHOCYTES OF PATIENTS WITH MALIGNANT LYMPHOGRANULOMA. (Ger.) Huber, C. (U. Innsbruck Med. Clin., Austria), H. Huber, F. Schmalzi, B. Lederer, D. Bütterich and H. Braunsteiner. Acta Haemat 44(4):222-232, 1970.

2585 STUDIES ON TRANSFER RNA^{Phe} FROM MORRIS 5123C HEPATOMA. (E.) Gonano, F. (Inst. Gen. Path., U. Modena, Italy) and G. Pirro. Cancer Res 31(5):656-657, 1971.

2586 CHROMOSOME ANALYSIS IN THE STUDY AND DIAGNOSIS OF BENIGN AND MALIGNANT EPITHELIAL TUMORS OF THE GASTROINTESTINAL TRACT. (It.) Messinetti, S. (Inst. Path. Surg., U. Rome, Italy) and M. Moscarini. Il Progresso Medico 26(24):721-724, 1970.

2587 CATECHOLAMINE METABOLISM IN THE TISSUE OF MALIGNANT AND BENIGN TUMORS. (Ger.) Käser, H. (Swiss Center Clin. Tumor Res., Tiefenau, Bern, Switzerland), K. Türlér and P. H. Burri. Schweiz Med Wschr 101(13):484-487, 1971.



ONSON, S.A.
2320, 2352, 2353
ALLA, A.M.
2374
L, C.A.
2443
ASHI, D.V.
2302
AHAM, S.
2553
ERMAN, L.V.
2165*
LBERG, M.
2402
ER, W.H.
2435
ENKO, A.I.
2333
JA, E.M.
2480
O, M.
2207
RICH, C.D.
2349
XANDER, P.
2406
EN, D.O.
2498
EN, P.
2499
SAADI, A.A.
2557
SARRAF, M.
2460
ER, M.
2485
HOFF, J.
2242, 2245
RUS, J.L.
2275
ERS, P.
2559
KI, K.
2293
OS, J.C.
2192
US, M.F.
2152, 2192
STRONG, G.R.
2302
STRONG, J.A.
2328
ADI, S.
2488
ANASIU, P.
2365

ATKIN, N.B.
2536
ATTARDI, G.
2528
ATTWOOD, M.M.
2303
AZAMA, Y.
2253
BABIUK, L.A.
2383
BACCHETTI, S.
2290
BACHENHEIMER, S.L.
2310
BACIGALUPO, G.
2223
BAESSLER, R.
2470
BALCHIN, L.A.
2406
BALDA, B.R.
2540
BALDWIN, R.W.
2426
BALL, J.K.
2178, 2225, 2266*
BARKER, K.L.
2551
BARRANCO, S.C.
2250
BARSKI, G.
2416
BARTLEY, J.C.
2553
BASILICO, C.
2382, 2388
BASSIN, R.H.
2351
BAUMAL, R.
2421
BEATY, A.
2186
BELEHRADEK, J., JR.
2416
BENDICH, A.
2224
BENIASHVILI, D.SH.
2196
BENSTED, J.P.M.
2256
BENTVELZEN, P.
2453
BERARD, C.W.
2493
BEREBBI, M.
2364

BERENBLUM, I.
2276, 2278
BERG, P.
2156
BERGOLITS, V.M.
2323
BERNFELD, M.R.
2475
BERNFELD, P.
2422
BERNSTEIN, I.D.
2440
BERSI, M.
2577*
BIEBER, R.E.
2422
BIGOTTI, A.
2200
BIKOFF, E.
2513
BIRKMAYER, G.D.
2540
BISHOP, J.M.
2357
BJOERK, G.R.
2508
BLAIR, D.G.R.
2509
BLAIR, P.B.
2160
BLAZEJ, T.
2204
BLOOM, B.
2421
BOBROV, YU.F.
2469
BOHLIG, H.
2481
BOLDEN, A.
2561
BOLIS, G.B.
2286
BOLOGNESI, D.P.
2312
BONMASSAR, A.
2448
BONMASSAR, E.
2448
BONNEAU, H.
2364
BOREK, E.
2511
BOROVIKOVA, N.M.
2294*
BORUM, K.
2455

BOWEN, J.M.
2400*
BOWEY, C.E.
2467
BOY, M.J.
2214
BRAUN, W.
2403
BRAUNSTEINER, H.
2584*
BREGA, A.
2570
BREGULA, U.
2514, 2554
BREIDENBACH, G.P.
2340
BRESNICK, E.
2547
BREWEN, J.G.
2203
BRIGGS, G.M.
2191
BROADATY, E.
2328
BROOKES, P.
2149
BROWN, D.Q.
2229
BRUCHER, J.M.
2247
BRUNI, J.E.
2501
BRYAN, W.R.
2366
BRYANT, G.M.
2192
BUCHALT, L.
2573*
BUECHNER, M.
2153
BUERKLE, G.
2184
BUETTERICH, D.
2584*
BUKIN, YU.V.
2317
BURG, C.
2432
BURLINGHAM, B.T.
2325
BURMESTER, B.R.
2310
BURNETT, J.B.
2541
BURNS, E.R.
2555

BURRI, P.H.
2587*
BURSTIN, S.J.
2382
BUSHONG, S.C.
2449
BUTEL, J.S.
2372
BUTLER, T.P.
2226
BUTLER, W.H.
2209, 2240
BUU-HOEI, N.P.
2269*
CAICUTS, M.
2505
CALAFAT, J.
2246
CAMBELOVA, J.
2417
CAME, P.E.
2346
CAMPBELL, J.A.
2387
CAPUTO, A.
2200
CARBON, J.
2148
CARBONE, P.
2535
CARDINI, G.
2577*
CASSINGENA, R.
2157
CATER, D.B.
2476
CESARINI, J.P.
2560
CHAN, E.W.
2178, 2266*
CHANG, N.H.
2458
CHECHELASHVILI, G.
2196
CHEN, J.K.M.
2268*
CHEN, K.
2425
CHEN, K.P.
2491
CHERNTSOVA, T.A.
2574*
CHIARUGI, V.P.
2529
CHOE, B.K.
2526

CHRISTOPHERSON, W.M.
2480
CIEGLER, A.
2267*
CIOLOCA, L.
2236
CLAFLIN, A.J.
2510
CLARK, E.
2522
CLARK, W.E., II
2566
CLIFFORD, P.
2305
CLINE, M.J.
2461
CLYMER, R.
2412, 2456
COCHRAN, A.J.
2314
COFFIN, D.L.
2230
COFFIN, J.M.
2358
COHEN, G.H.
2337
COHEN, S.
2451
COLEY, G.M.
2566
COONEY, D.A.
2186
CORY, J.G.
2321
COWDELL, R.H.
2467
CRATHORN, A.R.
2248, 2254
CROISY, A.
2269*
CRUMPACKER, C.S.
2332, 2371
CWYNARSKI, M.T.
2451
DAAMS, J.H.
2453
DABBERT, A.F.
2481
DABSKA, M.
2575*
DALQUEN, P.
2481
DALTON, A.J.
2302
DAMERAU, W.
2187

ANOV, I.
2478*
A, S.K.
2454
O, C.S.
2439
S, D.
2336
S, R.D.
2186
AULT, L.E.
2495
ERS, P.J.
2428, 2459, 2464*
ALLEUX, F.
2360
ARVEN, E.
2348
ORCO, R.T.
2509
ENGELSE, L.
2246
ORONHA, F.
2312
ME, K.B.
2191
I, L.S.
2515, 2530
DY, R.W.
2267*
SCH, A.
2517
Z, M.
2313
MAN, V.M.
2469
AOLO, J.A.
2197
HOWSKI, L.
2295, 2400*, 2410
FLER, W.
2325
A, Y.
2283
HEVA-STRATEVA, N.
2483
ER, M.
2432
VAN, P.J.
2197
C.R.
2288
IE, J.C.
2303
S, J.
2205

DRUCKREY, H.
2252, 2265*
DUSHKIN, V.A.
2166*
DVORAK, R.
2408, 2433
DZAGNIDZE, L.N.
2196
DZHIBILOV, I.I.
2166*
EBERT, J.D.
2164*
ECKHART, W.
2384
ECSENYI, M.
2571
EDGERTON, B.W.
2459
EDWARDS, J.G.
2387
EMBLETON, M.J.
2426
EMMELOT, P.
2246
ESTES, M.K.
2369
FAIRLEY, G.H.
2406
FANSHER, L.
2357
FARAS, A.
2357
FEDOROVA, A.V.
2294*
FEHER, J.
2180, 2182
FERSHTUDT, V.I.
2482
FIALKOW, P.J.
2305
FIESSINGER, J.N.
2445
FILBERT, J.E.
2298
FILCH, Y.H.
2428
FILITTI-WURMSER, S.
2445
FINGERHUT, B.
2572
FINK, L.M.
2199
FINK, M.A.
2409
FINKELSTEIN, M.
2263

FINOGENOVA, M.A.
2233
FISCHER, P.
2243
FISHER, B.
2462
FISHER, E.R.
2462
FISHMAN, W.
2567
FLETCHER, O.J.
2439
FLINT, G.L.
2261
FOLEY, G.E.
2494, 2515,
FONG, C.K.Y. 2530
2335
FOREMAN, C.
2457
FORNI, A.
2193
FORT, L.
2247
FOX, B.W.
2291
FRANKE, R.
2153
FRANKS, L.M.
2500
FRANZEN, S.
2531
FRIDLENDER, B.
2561
FRIED, W.
2277
FRIEDMAN, R.M.
2315
FRIEND, C.
2348
FRONGILLO, R.
2326
FUJIMURA, S.
2199
FUJINAGA, S.
2410
FUKUNAGA, F.H.
2486
FURST, A.
2195, 2268*
GAHRTON, G.
2494
GALLO, R.C.
2503
GANGADHARAN, P.
2487

GANTT, R.R.
2507
GARAPIN, A.C.
2357
GARDNER, M.B.
2298
GASPARINI, C.
2577*
GAZDAR, A.F.
2351
GEFTER, M.L.
2513
GELB, L.D.
2373
GELBOIN, H.V.
2168*
GHARPURE, M.
2327
GIBLETT, E.R.
2305
GIDALI, J.
2279
GILDEN, R.V.
2298, 2318, 2354,
2356, 2407, 2413,
2457, 2458
GILLIAVOD, N.
2281
GLAUMANN, H.
2237
GODWIN, M.C.
2257
GOERLICH, M.
2223
GOGICHADZE, G.K.
2319
GOLD, P.
2172*
GOLDBLUM, N.
2447
GOLDFEDER, A.
2348, 2405
GOLDIN, A.
2448
GOLDMAN, J.M.
2463*
GOLDSCHMIDT, B.M.
2204
GOLLMAR, Y.
2397*
GONANO, F.
2585*
GOOD, R.A.
2401
GOODHEART, C.
2296

GOODMAN, M.L.
2463*
GORDON, B.S.
2186
GORSKI, T.
2235
GOTHOSKAR, B.
2305
GOYANES-VILLAESCUSA, V.
2280
GRANBERG, I.
2525
GRANOFF, A.
2301
GRAVELL, M.
2338
GREEN, M.
2355
GREENAWALT, C.
2376
GREENBLATT, M.
2241
GREGORY, S.A.
2582*
GREY, H.M.
2443
GROVER, S.
2243
GRUNBERGER, D.
2199
GUETTNER, J.
2244
GURD, J.W.
2539
GURSEL, E.
2572
GUTMANN, H.R.
2183
GYOERKEY, F.
2558
GYOERKEY, P.
2558
HACKER, B.
2309
HAGHIGHI, P.
2488
HAHN, G.M.
2201
HAIN, E.
2481
HAKOMORI, S.I.
2359
HANCOCK, R.L.
2146
HARA, H.J.
2162

HARAN-G
24
HARD, G
22
HARDY,
23
HARO, R
22
HARRIS,
23
HARRY,
25
HARTMAN
24
HASLAM,
23
HATANAK
23
HATFIEL
25
HAWKS,
22
HAYAMIA
24
HEATH,
25
HEIDEL
22
HEILPER
22
HEINE,
23
HEISE,
22
HEMPEL
22
HENRY,
22
HENRY,
22
HESS,
22
HIBBER
22
HILDEB
22
HILDEM
22
HILF,
22
HILFRI
22
HILGER
22
HINZ,
22

C, H.C.
2379
NO, I.
2490
LIGETI, C.
2192
IANN, D.
2224, 2260
C.
2283
N, H.T.
2436
ND, J.C.
2213
S, V.W., JR.
2409
CZAK, J.A.
2329
J.
2538
K.H.
2238
ZEWICZ, J.S.
2307
NO, J.
2427
ELD, D.K.
2175*
ER, D.
2432
N, Z.
2496, 2545
G, G.D.
2335
C.C.
2307
E.S.
2369
C.
2584*
H.
2584*
MAN, E.
2221
N, J.B.
2383, 2392*
ER, G.
2163
ER, R.J.
2298, 2356, 2376,
2407, 2413, 2458
S, N.R.
2419
S, R.G.
2400*
Y.H.

2191
HULTIN, T.
2151
HUMPHREY, R.M.
2250
HUNTER, E.
2391
HYODO, M.
2546
IMAI, T.
2489
IRLIN, I.S.
2194, 2323, 2389
ITO, Y.
2381
IVANKOVIC, S.
2252
JACOB, A.
2214
JACQUIGNON, P.
2269*
JAENISCH, R.
2378
JAGATIC, J.
2257
JANNERS, M.Y.
2499
JENNINGS, E.H.
2180, 2182
JENNISSEN, H.
2427
JENSON, A.B.
2565
JOHNSON, G.S.
2315
JONAS, A.M.
2502
JONES, K.P.
2203
JOSE, D.G.
2401
JUDD, K.P.
2431
JUNGSTAND, W.
2244
JUSTUS, J.
2185
KACHI, H.
2490
KAESER, H.
2587*
KAKEFUDA, T.
2332, 2399*
KAPLAN, P.M.
2449
KARL, S.

2456
KARNAUKHOVA, E.N.
2219
KASHIMA, M.
2284
KATO, S.
2380, 2393*
KATO, T.
2490
KATZ, C.
2204
KAWAMURA, M.
2546
KAZANTSEVA, I.A.
2468
KEAST, D.
2316
KEDAR, E.
2447
KELEMEN, E.
2273*
KELLOFF, G.
2354, 2457,
KENNEY, F.T. 2458
2551
KERR, S.J.
2511
KERTSMAN, V.I.
2161
KHALATBARI, A.
2578*
KHOLMUKHAMEDOVA, N.
2333
KHUDOLEY, Y.V.
2167*
KHUNDANOVA, L.L.
2423
KIEFF, E.D.
2310
KIELER, J.
2420
KIM, U.
2275
KIMMEL, CH.B.
2450
KING, D.
2201
KIRSCHSTEIN, R.L.
2341
KLEIHUES, P.
2249
KLEIN, G.
2158, 2305,
2514, 2554
KLEIN, H.J. 2386,
2163

KLEINSASSER, O.
 2163
 KLEITKE, CH.
 2223
 KLOBUSICKA, M.
 2429
 KLOTZ, H.P.
 2173*
 KNOSPE, W.H.
 2582*
 KOBAYASHI, H.
 2411
 KODAMA, M.
 2368
 KOHNE, D.E.
 2373
 KOHSE, L.M.
 2392*
 KONDRATICK, J.
 2302
 KONIKOVA, E.
 2429
 KONSTANTINOV, V.G.
 2259
 KORENEVSKAYA, M.I.
 2574*
 KOSUT, V.
 2484
 KOTULOVA, D.
 2274
 KOURI, R.E.
 2229
 KOVACS, K.
 2217, 2227
 KOWALSKI, R.
 2576*
 KRAIN, L.S.
 2479
 KRAISELBURD, E.
 2336
 KRASNYANSKAYA, P.N.
 2196
 KRIEK, E.
 2181
 KROEGER, H.
 2427
 KRUG, H.
 2516
 KRUSH, A.J.
 2533
 KRUT'KOVSKAYA, N.P.
 2468
 KRYUKOVA, I.N.
 2367
 KUBO, T.
 2489

KULA, N.S.
 2210
 KURATSUNE, M.
 2202
 KURODA, K.
 2207
 KUWABARA, N.
 2253
 KUZMINYUK, A.I.
 2259
 KVEDAR, J.P.
 2366
 KYLE, R.A.
 2494
 LACOUR, F.
 2308
 LALLI, A.
 2562
 LAM, K.M.
 2335
 LAMB, M.J.
 2208
 LANDSCHUETZ, C.
 2252, 2265*
 LANGE, J.
 2312
 LAPPE, M.
 2424
 LAVRENT'YEV, L.N.
 2294*
 LAWRENCE, W.C.
 2337
 LE BRETON, E.
 2214
 LEDERER, B.
 2584*
 LEE, J.C.K.
 2550
 LEE, K.L.
 2551
 LEE, L.F.
 2310
 LE FRANCOIS, D.
 2416
 LEGALLAIS, F.Y.
 2306, 2341
 LEHRER, R.I.
 2461
 LEIBOWITZ, U.
 2485
 LEJEUNE, F.
 2438
 LEONARD, A.
 2281, 2524
 LEVIN, M.J.
 2332, 2371

LEVINE, A.
 2378
 LEVINSON,
 2357
 LEVY, J.A.
 2355
 LEWIS, A.
 2332
 LIEBELT,
 2547
 LIEBELT,
 2547
 LIJINSKY,
 2209
 LILLY, L.
 2208
 LIMA, J.F.
 2583
 LIMONTA,
 2193
 LIN, T.M.
 2497
 LINDNER,
 2408
 LING, R.C.
 2557
 LINKER-I,
 2430
 LINNIK, A.
 2222
 LITWACK,
 2518
 LOCKETT,
 2488
 LOG, T.S.
 2314
 LOHS, KH.
 2187
 LOONEY, J.
 2497
 LORENZ, I.
 234
 LUBET, R.
 222
 LUIPPOLD,
 220
 LUNDIN,
 248
 LUNGU, M.
 236
 LYNCH, H.
 253
 MAAG, T.
 230
 MAC MAHO,
 249

HERSON, I.A.
2155, 2361, 2477
PAA, P.H.
2475
E, P.N.
2150
ROVA, G.F.
2389
JKA-GIGANTI, D.
2183
EL, L.R.
2309
J.
2336
ANI, M.
2380, 2393*
J.
2519, 2525
EWITZ, M.
2535
OR, J.
2518
JARDT, H.
2218, 2224
ANI, A.
2269*
EN, M.A.
2373
YAMA, K.
2295
YAMA, Y.
2289
DA, Y.
2202
VINOVIC, J.
2562
JOKA, O.
2284
JZAWA, T.
2282
ELIN, G.
2496
ELL, K.W.
2261
IELD, E.D., JR.
2547
A.A.
2499
RENKO, N.P.
2319
LISTER, R.M.
2298
ARTER, J.A.
2225
ORMICK, K.J.
2343

MC DONALD, S.
2327
MC GRATH, H.
2553
MC GRATH, L.
2392*
MC INTYRE, N.
2548
MC KINNIE, K.L.
2557
MC MILLAN, V.L.
2449
MEDRAS, K.
2190
MEDZIHRADESKY, J.
2429
MELCHIONNE, S.
2204
MELLON, J.G.
2499
MENDEZ, W.M.
2480
MERANZE, R.D.
2495
MERKOW, L.P.
2330
MERRICK, S.
2425
MESSINETTI, S.
2586*
METCALF, D.
2404
MEYER, G.
2437
MEYERS, P.
2436
MILLER, D.
2463*
MINOWADA, J.
2307
MIRVISH, S.
2241
MITTELMAN, A.
2520
MIWA, K.
2251
MIYAMOTO, K.
2318
MIZELL, M.
2340
MIZUKAMI, T.
2251
MIZUTANI, S.
2368
MOCHIZUKI, Y.
2495, 2545

MOHALLATEE, E.A.
2488
MOHR, U.
2242, 2245
MONTEMURRO, D.G.
2501
MOORE, D.H.
2346
MORA, P.T.
2198
MORGAN, J.F.
2509
MORI, M.
2381
MORISHITA, M.
2381
MORRIS, H.P.
2495, 2498, 2499,
2512, 2545, 2548
MOSCARINI, M.
2586*
MOSKOVKINA, O.YA.
2323
MUELLER, D.
2564
MUENCH, K.H.
2510
MUMFORD, D.M.
2343
MUNSHOWER, J.
2498
MUNYON, W.
2336
MURAMATSU, E.
2284
MYERS, B.
2410
NABIZADEH, I.
2488
NACHTIGAL, M.
2372
NAEGELE, R.F.
2301
NAGEL, G.A.
2438, 2466*
NANDI, S.
2345, 2349
NASH, M.A.
2400*
NASTAC, E.
2365
NATHANSON, L.
2567
NAVARRETTE, A.R.
2568
NAZERIAN, K.

2310
 NEAL, J.
 2258
 NEGRONI, G.
 2391
 NEIDHARDT, F.C.
 2508
 NELSON, R.L.
 2197
 NEUMANN, H.G.
 2271*
 NEVSKAYA, T.P.
 2574*
 NEWBERNE, P.M.
 2210
 NEY, R.L.
 2537
 NEYMAN, I.M.
 2176*
 NICHOLLS, E.M.
 2583*
 NICHOLSON, M.O.
 2298
 NII, S.
 2334
 NILSSON, A.
 2285
 NISHIYAMA, R.H.
 2562
 NORDEN, A.
 2517
 NORRBY, E.
 2397*
 NOSNY, M.A.
 2437
 NOVOTNA, L.
 2429
 NOWAKOWSKI, T.K.
 2576*
 NOWINSKI, R.C.
 2395*
 OBUKH, I.B.
 2367
 OCHIAI, M.
 2270*
 O'CONOR, G.T.
 2341
 O'DONNELL, P.V.
 2395*
 OGINO, T.
 2324
 OHYAMA, H.
 2293
 OJALA, D.
 2528
 OKANO, H.

2347
 OKUMURA, Y.
 2282
 OLD, L.J.
 2395*
 OLIVER, J.A.
 2374
 OLLIER, M.P.
 2445
 OLWENY, C.L.M.
 2493
 O'NEILL, F.J.
 2339, 2342
 ONO, T.
 2546
 ORAVEC, C.
 2417
 ORIEL, J.D.
 2396*
 OROSZLAN, S.
 2356, 2407, 2457,
 2458
 OSIPOV, N.YE.
 2319
 OSTROWSKI, K.
 2420
 OSTRYANINA, A.D.
 2234
 OTAKI, N.
 2542, 2543
 OTIS, R.D.
 2566
 OXFORD, J.S.
 2303, 2331
 OXMAN, M.N.
 2371
 PACIFICO, E.
 2193
 PAGANO, J.S.
 2369
 PAI, S.R.
 2552
 PALMER, M.S.
 2230
 PARDO, M.
 2330
 PARKER, J.E.
 2480
 PARKHOMENKO, I.I.
 2194
 PASCOE, J.M.
 2248, 2254
 PASTAN, I.
 2315
 PATOKIN, S.V.
 2469

PAULUZZI,
 2326
 PAYMASTER
 2487
 PAYNE, R.E.
 2375
 PEARSON, F.
 2203
 PEARSON, C.
 2226
 PEGG, A.E.
 2216
 PEILLON, F.
 2580*
 PELLAR, J.
 2576*
 PELLETIER,
 2580*
 PERCY, D.H.
 2502
 PERLMUTTER
 2522
 PERRY, S.
 2170*
 PETERKOFSK
 2518
 PETERSON,
 2291
 PHAN, H.H.
 2214
 PHAN HUN T
 2580*
 PHILLIPS,
 2218,
 PHILLIPS,
 2316
 PICK, C.R.
 2476
 PIESSENS,
 2438
 PILCH, Y.H.
 2459,
 PILLINGER,
 2474
 PIRRO, G.
 2585*
 PITOT, H.C.
 2549
 PLAGEMANN,
 2544,
 PLANT, J.E.
 2248
 PLESKA, O.
 2403
 POISSANT,
 2562

MAR'KOV, V.I.
2319
SCU, N.C.
2236
JGAL, F.H.
2505
J.E.
2312
ER, A.M.
2331
ER, C.W.
2303, 2331
ER, V.R.
2549
S, R.L.
2406
J.W.
2443
SMAN, D.
2415
SMANN, R.
2252
ST, H.
2579*
P.C.
2214
ON, A.S.
2306, 2341
KHIN, A.YE.
2472
OOT, J.
2580*
ETEN, N.
2186
ING, K.P.
2464*
IVE, K.J.
2552
ERATH, K.
2527
IE, I.
2180, 2182
F.
2339, 2342, 2565
H.J.
2440
A, K., JR.
2329
OVA, J.
2403
HENBAKH, M.O.
2317
CH, A.
2394*
K.K.
2362

REIF, A.
2465*
REIF, A.E.
2414
REILLY, C.A.
2322
RENZETTI, A.D., JR.
2261
REUBER, M.D.
2549
REUTER, A.M.
2497
REVAZOVA, YE.S.
2319
REYNOLDS, R.D.
2549
RHIM, J.S.
2376
RIBACCHI, R.
2326
RICE, J.M.
2263
RICH, M.A.
2313, 2412, 2456
RICHARDS, A.H.
2222
RICHTER, G.W.
2550
RICKARD, C.G.
2312
RIGDON, R.H.
2258
RIOU, G.
2308
RIZZO, A.J.
2262
RJOSK, H.K.
2271*
ROBBINS, P.W.
2477
ROBERTS, J.J.
2248, 2254
ROBINSON, W.S.
2398*
ROBINSTON, H.L.
2398*
ROGERS, A.E.
2210
ROIZMAN, B.
2310
ROKUTANDA, H.
2355
ROKUTANDA, M.
2355
RONGEY, R.W.
2298

ROSAI, J.
2165*
ROSCHLAU, G.
2185
ROSS, J.
2320
ROWE, W.P.
2332, 2371
RUDALI, G.
2171*
RUSSELL, E.
2351
RUSSELL, W.C.
2328
RYDEL, R.E.
2183
SACKSTEDER, M.R.
2366
SAINT CYR, C.DE V.
2437
SAITO, T.
2359
SAKAUE, Y.
2393*
SALAK, D.
2499
SALZMAN, L.A.
2300, 2399*
SANDBERG, A.A.
2175*
SANDER, J.
2184
SANDERS, F.K.
2395*
SARDESAI, S.
2460
SARMA, P.S.
2311, 2413
SAUER, G.
2377
SAVLUCHINSKAYA, L.A.
2239
SCANLON, M.D.
2400*
SCHAEFER, D.
2473
SCHAEFER, W.
2312
SCHAEFFER, B.T.
2206
SCHARFF, M.D.
2421
SCHAUDIG, G.
2573*
SCHEIN, P.S.
2186

SCHER, C.D.
2370
SCHERMULY, W.
2473
SCHIEFER, H.G.
2163
SCHLABACH, A.
2561
SCHLAUDER, M.C.
2195
SCHLOSS, G.T.
2322
SCHMALZI, F.
2584*
SCHMICKEL, R.D.
2375
SCHMIDT, A.
2244
SCHNEIDER, R.
2288
SCHOENTAL, R.
2256
SCHOLEFIELD, P.G.
2539
SCHORR, I.
2537
SCHRAMM, T.
2187
SCHREMMER, C.N.
2238
SCHULZ, W.D.
2272*
SCHWARTZ, R.D.
2366
SCOLNICK, E.M.
2320
SEGEV, Y.
2402
SEIDLOVA, A.
2538
SEIDLOVA, B.
2465*
SEIJI, M.
2542, 2543
SELKIRK, J.K.
2221
SELLYEI, M.
2273*
SERGEYEV, A.V.
2317
SHABAD, L.M.
2228, 2239
SHARMA, O.K.
2511
SHAW, M.W.
2174*

SHEARER, R.W.
2212
SHEID, B.
2512
SHER, A.
2444
SHUGART, L.R.
2521
SIBAL, L.R.
2409
SICILIANO, M.J.
2522
SIGEL, M.M.
2436
SINCLAIR, W.K.
2290
SINKOVICS, J.G.
2558
SIVAK, A.
2204
SJOEGREN, H.O.
2455
SKINNER, M.S.
2340
SLESERS, A.
2495, 2545
SLIFKIN, M.
2330
SMIDA, J.
2363
SMIDOVA, V.
2363
SMIECINSKI, W.
2235
SMIRNOV, G.A.
2228
SMITH, B.A.
2254
SMITH, C.E.
2198
SMITH, H.S.
2370
SMITH, M.
2568
SMITH, M.N.
2565
SMITH, P.D.
2581*
SMITH, R.T.
2435
SMULLYAN, I.
2188
SO, B.T.
2241
SOMOGYI, A.
2217, 2227

SONTAG, J.M.
2276, 2278
SOROKINA, YU.D.
2231
SOSNIK, H.
2190
SPAIN, J.D.
2213
SPEAR, P.G.
2310
SPIEGELMAN, S.
2299
SPJUT, H.J.
2565
SPORN, M.B.
2179
SPRIGGS, A.I.
2467
SPRYSHKOVA, M.A.
2220
SQUARTINI, F.
2286, 2344
SQUIRES, C.
2148
STANLEY, N.F.
2316
STAUGAARD-KLOOSTERZIJ
2556
STAVRAKY, K.M.
2264
STEFANOVIC, J.
2274
STENBACK, W.A.
2343
STEPHENS, K.
2431
STERN, K.
2405
STERNBERG, S.S.
2218
STILMANT, M.M.
2438
STJERNSWAERD, J.
2418
STOFFYN, P.
2563
STOIAN, M.
2365
STOKER, M.
2390
STONE, L.B.
2297
STROHL, W.A.
2329
STRYCKMANS, P.
2563

TULBERG, M.P.
 2521
 TURROCK, J.E.
 2248
 UDAREV, P.V.
 2161
 UGIMOTO, T.
 2211
 UGIMURA, T.
 2253
 ULITZEANU, A.
 2402
 ULITZEANU, S.
 2447
 UN, S.C.
 2206
 UNDERMAN, F.W., JR.
 2154
 UROWIAK, J.
 2287
 VEJDA, J.
 2484
 WANSON, D.H.
 2230
 WEARINGEN, G.R.
 2410
 WIFT, M.
 2534
 AGUCHI, S.
 2293
 AKADA, A.
 2275
 AKADA, Y.
 2275
 AKAHASHI, M.
 2324
 AKAMATSU, O.
 2251
 AKASUGI, M.
 2442
 AKAYAMA, S.
 2253
 AKEMOTO, K.K.
 2297, 2376
 AKIGUCHI, T.
 2435
 APER, H.S.
 2247
 ARIKAS, H.
 2444
 AYLOR, D.O.N.
 2288
 AYLOR, M.W.
 2526
 AYLOR-PAPADIMITRIOU, J.
 2390

TCHOU, H.P.
 2510
 TELLER, M.N.
 2188
 TEMIN, H.M.
 2358, 2368
 TEMPLETON, A.C.
 2492, 2493
 TERAYAMA, H.
 2211
 TERENTIEVA, E.I.
 2574*
 TER-GRIGOROV, V.S.
 2323
 TEVETHIA, S.S.
 2372, 2449
 THOMAS, B.S.
 2459
 THOR, D.E.
 2440
 TODARO, G.J.
 2320, 2370
 TOMASULO, J.
 2569
 TOT, F.
 2367
 TOURNIER, P.
 2157
 TRAININ, N.
 2276, 2278, 2430
 TRALKA, T.S.
 2341
 TRENTIN, J.J.
 2343, 2431
 TRIBUKAIT, B.
 2531
 TUERLER, K.
 2587*
 TURKINGTON, R.W.
 2506
 TURKIYA, N.B.
 2196
 TURNER, H.C.
 2413
 TURUSOV, V.S.
 2219
 TYRRELL, S.A.
 2306
 ULLAND, B.
 2263
 UNGER, E.
 2279
 UPITER, M.Z.
 2472
 USSERY, M.A.
 2400*

USTACELEBI, S.
 2327
 VAAGE, J.
 2425
 VADLAMUDI, S.
 2448
 VAITKEVICIUS, V.K.
 2460
 VANDEPUTTE, M.
 2454
 VAN DER MEER, J.
 2556
 VAN DUUREN, B.L.
 2204
 VANKY, F.
 2418
 VASIL'YEVA, N.H.
 2189
 VAUGHAN, R.K.
 2337
 VEENEMA, R.J.
 2572
 VESCO, C.
 2570
 VIALE, G.L.
 2523
 VIELKIND, J.
 2559
 VIELKIND, U.
 2559
 VIGIL, E.L.
 2545
 VIOLA, P.L.
 2200
 VISFELOT, J.
 2531
 VLCEK, B.
 2465*
 VOGT, P.K.
 2359, 2366
 VOLEGOV, A.I.
 2232
 VOLGAREV, M.N.
 2471
 VOLKERS, S.A.S.
 2526
 VORONIN, E.S.
 2166*
 VOUTE, P.A., JR.
 2556
 WAGNER, L.
 2205
 WAINFAN, E.
 2304
 WAKABAYASHI, K.
 2546

WALKER, D.L.
2379
WALLACE, J.H.
2340
WALTERS, M.N.I.
2316
WANG, R.
2388
WARREN, J.
2366
WARTENBERG, J.
2576*
WATANABE, T.
2415
WEBB, D.
2403
WEBB, T.E.
2262
WEBER, G.
2498
WEI, R.D.
2206
WEINSTEIN, E.B.
2199
WEISBURGER, E.K.
2255, 2263
WEISBURGER, J.H.
2255, 2263
WEISS, D.W.
2402
WEISSBACH, A.
2561
WELLS, R.T.
2368
WERNER, W.
2578*
WHIMSTER, I.W.
2396*
WHITE, H.J.
2555
WHITE, L.E.
2192
WHITE, W.L.
2399*
WIENER, F.
2386, 2554
WIENER, M.
2447
WILDNER, G.P.
2215
WILKINSON, R.
2474
WILLIAMS, J.F.
2327, 2387
WILLIAMS, W.C.
2410

WILSON, P.D.
2500
WILSON, R.
2242
WILSON, S.M.
2512
WITTIG, G.
2215
WITZ, I.P.
2441
WOGAN, G.N.
2207
WOLBERG, W.H.
2452
WOLF, M.
2238
WU, C.
2557
WULFF, U.C.
2530
WYKE, J.
2385
WYNDER, E.L.
2260
YABLONSKAYA, L.YA.
2220
YABLONSKI, M.
2485
YAGI, Y.
2415
YAKOVLEVA, L.S.
2169*
YAMADA, T.
2293
YAMAMOTO, K.
2292
YAMAMOTO, R.S.
2255
YAMANOUCHI, K.
2446
YANG, S.J.
2201
YANG, W.K.
2504
YASHPHE, D.J.
2159
YOON, C.H.
2422
YOSHIDA, T.O.
2381
YOSHIKAWA-FUKADA, M.
2164*
YOSHIMURA, Y.
2381
YOST, Y.
2183

YOUN, J.K.
2416
YOUNG, L.
2402
ZAMECNIK, P.
2147
ZANG, K.D.
2532
ZANK, M.
2516
ZANKL, H.
2532
ZAPOL'SKAYA,
2294*
ZAWARTKA, M.
2576*
ZAWIRSKA, B.
2190
ZBAR, B.
2440
ZEIKUS, J.G.
2526
ZEPPA, M.P.
2326
ZHAROVA, YE.
2319
ZIEBARTH, D.
2215
ZIEGLER, J.L.
2493
ZIMMERMAN,
2329
ZIMMERMANN,
2177*
ZSCHIESCHE,
2272*

-ACETOXY-2-ACETYLAMINOFLUORENE
 TRNA, GUANOSINE (2199)
 -ACETYLAMINOFLUORENE
 HEPATOMA, RESISTANCE, RAT (2426)
 LIVER CARCINOMA, PORPHYRINS,
 RAT (2190)
 DENOCARCINOMA
 ENDOMETRIUM, PROTEIN SULFHYDRYL
 GROUPS, HUMAN (2468)
 FLATOXIN
 B1, HEPATECTOMY, RNA SYNTHESIS,
 LIVER, RAT (2205)
 B1, KIDNEY, RNA POLYMERASE,
 MOUSE (2207)
 B1, LIVER CARCINOMA,
 HEPATECTOMY, RAT (2210)
 B1, MUTAGENESIS, DROSOPHILA
 (2208)
 BIOSYNTHESIS, METHIONINE
 ANALOGS (2267)*
 CIRRHOSIS, CARCINOGENESIS,
 LIVER, RAT (2206)
 G1, LIVER, RAT (2209)
 LKYLATING AGENT
 DNA, REPAIR SYNTHESIS, HELA,
 HAMSTER (2254)
 DNA, RNA, REPAIR, HELA (2248)
 NTIBIOTIC
 EXORIBONUCLEASE, RNA, EHRLICH'S
 ASCITES TUMOR (2179)
 NTIBODY
 ANTILYMPHOCYTE SERUM, LYMPHO-
 CYTES, SARCOMA, MICE (2442)
 ANTILYMPHOCYTE SERUM, SPON-
 TANEOUS LYMPHOMA, MOUSE
 (2431)
 COMPLEMENT, EHRLICH'S ASCITES
 TUMOR, NORMAL HUMAN SERUM
 (2417)
 HERPES SIMPLEX VIRUS,
 PERSISTENCE, EARLE'S L CELLS,
 HUMAN (2334)
 LEUKEMIA STAGES, L1210, MOUSE
 (2448)
 MYELOMA, MOUSE TISSUE (2414)
 NTIGEN
 2-ACETYLAMINOFLUORENE,
 HEPATOMA, RESISTANCE, RAT
 (2426)
 CARCINOEMBRYONIC, REVERSION,
 HUMAN (2172)*
 CELL MEMBRANE, SV40, KIDNEY
 (2447)
 DIMETHYLAMINOAZOBENZENE,
 HEPATOMA, RAT (2423)
 FERRITIN, VIRUS PARTICLE,
 MAMMARY TUMOR, MOUSE (2347)
 GROUP SPECIFIC, C-VIRUS,
 LEUKEMIA, RODENT (2457)
 GROUP SPECIFIC, FELINE LEUKEMIA
 VIRUS, ISOLATION (2312)
 MAMMARY TUMOR VIRUS, BLOOD,
 TISSUE, MICE (2349)
 MURINE SARCOMA VIRUS (2458)
 SARCOMA, MIGRATION INHIBITION,
 MICE (2420)
 SERUM, LYMPHOID TUMOR, CHICKEN
 (2439)
 SERUM, MAMMARY CANCER, MURINE
 (2422)
 SHEEP ERYTHROCYTES, HAMSTER
 CELLS, VIRUS, GLYCOPROTEINS
 (2437)
 SPECIFICITY, INTRASPECIES,
 INTERSPECIES, C-TYPE VIRUSES
 (2407)
 SUBUNITS, HEMAGGLUTINATION-INHIBITION
 ASSAY, RAUSCHER LEUKEMIA VIRUS
 (2409)
 SURFACE, MYELOMA, CYTOTOXICITY, MOUSE
 (2415)
 TUMOR, CELL CLONES, POLYOMA VIRUS,
 MOUSE (2391)
 TUMOR, POLYOMA VIRUS, RAT (2454)
 VIRUS, MOUSE, HAMSTER, CAT, C-TYPE
 (2356)
 AROMATIC HYDROCARBON
 CARCINOGENICITY, ELECTRON TRANSFER
 ENERGIES, HYDROPHOBIC PROTEIN
 BINDING (2153)
 POLYCYCLIC, CARCINOGEN BINDING,
 DNA TEMPLATE (2266)*
 ASBESTOS
 FERRITIN, MESOTHELIOMA, LUNG, ABDOMEN,
 HUMAN (2257)
 ASCITES
 EHRLICH, ANTIBODIES, COMPLEMENT,
 HUMAN SERUM (2417)
 BACILLUS CALMETTE-GUERIN
 3-METHYLCHOLANTHRENE, CARCINOGENESIS,
 MOUSE (2272)*
 METHYLCHOLANTHRENE, RATS, MICE, TUMOR
 TISSUE (2238)
 BACTERIOPHAGE
 TRANSFER RNA, E. COLI (2513)
 BENZ(C)ACRIDINES
 DNA, DIMETHYL DERIVATIVES, INTERACTION
 (2178)
 BENZENE
 GRANOLYCYTIC LEUKEMIA, CHROMOSOME

- STUDY (2273)*
 TOLUENE, OCCUPATIONAL HAZARD, CHROMOSOME CHANGES (2193)
- BENZO(A)PYRENE
 AIRPLANE ENGINE SOOT, MOUSE (2228)
 BROILED OIL, CARCINOGENICITY, RAT (2196)
 COCARCINOGEN, TOBACCO, SKIN, MOUSE (2204)
 HYDROXYLASE, LUNG, HAMSTER (2230)
 LUNG, UPTAKE, HAMSTER (2229)
 OCCUPATIONAL HAZARD, ALUMINIUM PLANT (2259)
 POLLUTION, FIBROSARCOMA, MOUSE (2258)
 PYRENE, TRANSPLACENTAL ACTION, KIDNEY TISSUE, MOUSE (2231)
 RNA, IMMUNITY, SARCOMA, RAT (2428)
 SMOKED FISH, JAPAN, DIET (2202)
- BLOOD
 VESSELS, PLASMINOGEN, GRANULOMAS (2476)
- BONE MARROW
 PROLIFERATION, LEUKEMIA (2170)*
- BRAIN
 CEREBELLUM, 7,12-DIMETHYLBENZ(A) ANTHRACENE, TUMOR MODEL, RAT (2220)
 HYPOPHYSIS, MORPHOLOGY, TUMOR, RAT (2580)*
 HYPOTHALAMUS, MAMMARY GLAND, TUMOR, MOUSE (2501)
 TRANSFER RNA, BASE COMPOSITION (2527)
 TUMOR, TRNA, METHYLASE (2523)
- BURKITT'S LYMPHOMA
 FOREIGN CELL CONTAMINATION (2305)
 HERPES-LIKE VIRUS PARTICLES, ANTIGEN, MAN (2343)
 IMMUNOGLOBULINS, ISOANTIGENS, HUMAN (2158)
 INFECTIOUS MONONUCLEOSIS, LEUKEMIA, CELL POPULATION (2494)
 INHIBITION, HERPESVIRUS HOMINIS, VIRUS (2306)
- CAPSID
 ADENOVIRUS TYPE 3,9,4,6, COCULTIVATION (2397)*
- CARBOHYDRATE
 METABOLISM, ADENOVIRUS TYPE-12, RAT (2333)
- CARCINOGENICITY
 FOOD, ADDITIVES, REVIEW (2176)*
- CARCINOMA
 LEUKEMIA, COMBINED CASES (2578)*
- CELL
 FUSION, VIRUS, MURINE LEUKEMIA (2315)
 LEUKEMIA, IMMUNOLOGY, HUMAN (2406)
- PROLIFERATION, POLYOMA VIRUS, MURINE (2389)
 SUSPENSION, SURFACE INTERACTIONS, POLYOMA VIRUS (2387)
- CERVIX
 HYPERPLASIA, ORAL CONTRACEPTIVES (2478)*
 MUCOUS LUBRICATION, 3-METHYLCHOL-ANTHRENE, MOUSE (2235)
 PRECANCEROUS CONDITION, CHROMOSOME (2467)
- CHEMICAL CARCINOGEN
 AROMATIC HYDROCARBONS, ELECTRON TRANSFER ENERGY, HYDROPHOBIC PROTEIN BINDING, STATISTICAL ANALYSIS (2153)
 DIETHYLNITROSAMINE, FISH, REVIEW (2167)*
 DNA BINDING (2149)
 GENETIC ACTION, HUMAN ENVIRONMENT (2168)*
 LIVER, PROTEIN SYNTHESIS (2151)
 POLYCYCLIC THIAZOLE CARCINOGENS (2269)*
- CHOLESTEROL
 BIOSYNTHESIS, MORRIS HEPATOMA (2548)
- CHROMATIN
 RNA, LIVER, HEPATOMA, RAT (2198)
- CHROMOSOME
 ABERRATION, EPSTEIN BARR VIRUS (2307)
 ABERRATION, POLYCYTHEMIA, HUMAN (2531)
 ABERRATION, X-IRRADIATION, RABBIT, HUMAN (2280)
 ABNORMALITY, LEUKEMIA (2577)*
 ABNORMALITY, LEUKEMIA, REVIEW, HUMAN (2175)*
 ABNORMALITY, VIRUS, HERPES SIMPLEX (2342)
 ASCITES TUMOR, MOUSE (2538)
 CELL FUSION, L CELLS, EHRlich, ASCITES (2554)
 CHANGES, TOLUENE, BENZENE, OCCUPATIONAL HAZARD (2193)
 DAMAGE, CHEMICAL, REVIEW, HUMAN (2174)*
 DAMAGE, X-IRRADIATION, 131I, HUMAN (2283)
 DNA, OVARIAN NEOPLASIA, HUMAN (2536)
 FIBROBLASTS, SARCOMA, HYBRIDIZATION, MURINE (2386)
 GASTROINTESTINAL TRACT, TUMOR (2586)*
 HYBRIDIZATION, EHRlich TUMOR, TUMORIGENICITY (2514)
 LEUKEMIA, PANCYTOPENIA, BENZENE (2273)*

MENINGIOMA, HUMAN (2519)
 PHILADELPHIA, MENINGIOMA, HUMAN (2532)
 PRECANCEROUS CONDITION, CERVIX, HUMAN
 (2467)
 RHABDOMYOSARCOMA, DOUBLE-MINUTE,
 HUMAN (2525)
 ROUS SARCOMA VIRUS, POLYOMA VIRUS,
 HAMSTER CELLS (2364)
 TRISOMY, SV40, SUSCEPTIBILITY (2375)
 TUMOR, POLYPASSAGE, 3-METHYLCHOL-
 ANTHRENE, HAMSTER (2236)
 N
 CARCINOMA, DIMETHYLHYDRAZINE, INGESTA,
 RATS (2215)
 LEUKEMIA, FAMILY 'G', INCIDENCE
 (2533)
 ON OIL
 BETA-GLUCURONIDASE, RAT (2180)
 MAST CELL, INFLAMMATION, RAT (2182)
 SIN
 DIET, LIVER, MORTALITY (2490)
 AMATE
 SACCHARIN, ENVIRONMENTAL FACTOR,
 CARCINOGENICITY, REVIEW (2171)*
 OHEXYLAMINE
 MUTAGENESIS, LEUKOCYTE, HUMAN (2203)
 OPHOSPHAMIDE
 LUNG ADENOMA, CARCINOMA,
 TRANSPLACENTAL EFFECT, MOUSE (2185)
 GENETICS
 LEUKEMIA, HUMAN, ACUTE GRANULOCYTIC
 (2582)*
 SINE ARABINOSIDE
 HERPES SIMPLEX, CHROMOSOME CHANGES,
 HUMAN (2339)
 TOXICITY
 SPLEEN CELLS, RHABDOMYOSARCOMA, MOUSE
 (2432)
 YCHOLATE
 CANCER IMMUNITY, HUMANS, ANIMALS
 (2465)*
 NZ(A,H)ANTHRACENE
 METABOLISM, EPOXIDE INTERMEDIATE,
 LIVER, RAT (2221)
 CIRRHOSIS, LIVER CARCINOMA, RAT (2471)
 IMMUNITY, TUMOR HETEROGRAFT, RAT
 (2401)
 SMOKED FISH, JAPAN, BENZO(A)PYRENE
 (2202)
 HYLAMINOETHYL-DEXTRAN
 MURINE SARCOMA VIRUS, TUMOR
 ENHANCEMENT (2351)
 HYLNITROSAMINE
 LIVER, SPLEEN, KARYOTYPE, RAT (2243)

LUNG ADENOMA, HEPATIC DAMAGE, MICE
 (2245)
 TRACHEA, HAMSTER (2242)
 DIFFERENTIATION
 PAPILLARY FOLLICULAR THYROID TUMOR,
 IMPLANTS, RAT (2562)
 DIMETHYLAMINOAZOBENZENE
 ANTIGENS, HEPATOMA, RAT (2423)
 TUMOR, HEPATECTOMY, HYPERTROPHY,
 RAT (2214)
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 ADRENAL LESION, MUSCULAR STRESS, RAT
 (2217)
 CEREBELLUM, TUMOR MODEL, RAT (2220)
 1,2,5,6-DIBENZANTHRACENE, IONIZING
 IRRADIATION, RARE EARTH METALS, RAT
 (2294)*
 DNA, CARCINOGEN BINDING, RAT LIVER
 (2224)
 HORMONE, REGRESSION, PROLACTIN, RAT
 (2226)
 LIVER, HEPATECTOMY, RAT (2218)
 MAMMARY GLAND, FIBROADENOMA, LACTOSE,
 RAT (2223)
 MAMMARY NEOPLASIA, ISOENZYMES,
 OOPHORECTOMY, RAT (2222)
 MAST CELLS, MAMMARY TUMORS, RAT (2227)
 3-METHYLCHOLANTHRENE, POLYOMA VIRUS,
 CELL GROWTH, IN VITRO, HAMSTER
 (2194)
 POLYINOSINIC-POLYCYTIDYLIC ACID,
 LYMPHOMA, THYMUS, MOUSE (2225)
 SKIN MORPHOLOGY, MOUSE (2189)
 X-RAY IRRADIATION, SKIN TUMOR, RAT
 (2219)
 DIMETHYLHYDRAZINE
 COLONIC CARCINOMA, INGESTA, RATS
 (2215)
 1,2-DIMETHYLHYDRAZINE
 ENZYME, TRNA METHYLASE, COLONIC TUMOR,
 MOUSE (2216)
 DIMETHYLNITROSAMINE
 TESTIS, RAT (2240)
 ULTRASTRUCTURE, LUNG, LIVER, MOUSE
 (2246)
 DIMETHYLSULFOXIDE
 CARCINOGENICITY, NEGATIVE, RAT (2187)
 DISEASE
 PRECURSOR ILLNESS, LUNG CANCER (2264)
 DNA
 ADENOVIRUS 12, SIZE CLASSES (2325)
 ALKYLATING AGENTS, REPAIR SYNTHESIS,
 HELA (2254)
 BENZ(C)ACRIDINES, DIMETHYL DERIVATIVE,
 INTERACTION (2178)

CARCINOGENS, BINDING (2149)
 CHROMOSOME, OVARIAN NEOPLASIA, HUMAN (2536)
 HEPATOMA, GENE AMPLIFICATION, RAT (2212)
 LEUKEMIA, CHROMOSOME, HUMAN (2564)
 LIGASE, EXONUCLEASE, ROUS SARCOMA VIRUS (2368)
 LIVER, CARCINOGEN BINDING, 7,12-DIMETHYLBENZ(A)ANTHRACENE, RAT (2224)
 MAREK'S DISEASE VIRUS (2310)
 5-METHYLCYTOSINE, LEUKEMIC CELLS, HUMAN (2530)
 MITOCHONDRIA, VIRUS, AVIAN MYELOBLASTOSIS, OLIGOMER (2308)
 MOLECULAR WEIGHT, TRITIATED THYMIDINE, LYMPHOMA, MOUSE (2291)
 POLYMERASE, HELA, WI38 (2561)
 POLYMERASE, KILHAM RAT VIRUS (2300)
 POLYMERASE, ROUS SARCOMA VIRUS, CHICKEN CELL (2358)
 POLYMERASE, ROUS SARCOMA VIRUS, DEFECTIVE (2398)*
 PRIMARY TUMOR, METASTASIS, HUMAN (2516)
 QUANTITATION, SV40 VIRUS-TRANSFORMED CELL (2373)
 RNA, ALKYLATING AGENTS, REPAIR, HELA (2248)
 RNA, NUCLEIC ACID METHYLASES (2150)
 RNA VIRUSES (2299)
 SV40, ADENOVIRUS 2, HYBRID VIRUS (2332)
 SV40, OLIGOMERS (2378)
 SYNTHESIS, HERPES SIMPLEX, KB CELLS (2337)
 SYNTHESIS, HYDROCORTISONE, LIVER, RAT (2262)
 SYNTHESIS, LYMPHOCYTES, LYMPHO-GRANULOMA (2584)*
 SYNTHESIS, ROUS SARCOMA VIRUS, IN VITRO (2357)
 SYNTHESIS, X-IRRADIATION, HAMSTER CELLS (2290)
 TEMPLATE, CARCINOGEN BINDING, POLYCYCLIC AROMATIC HYDROCARBONS (2266)*
 TUMOR, EHRlich ASCITES (2579)*
 UNSCHEDULED SYNTHESIS, MUSCLE, RAT (2201)
 VIRAL GENOME, TRANSFORMATION (2156)
 VIRUS, KILHAM RAT (2399)
 VIRUS, SIMIAN ADENOVIRUS, DENSITY (2296)

EMBRYO
 KIDNEY, BENZO(A)PYRENE, MOUSE (2231)
 ENDOCRINE GLAND
 CARCINOMA (2173)*
 TUMOR, PATHOGENESIS, ADRENAL CORTEX, REVIEW (2161)
 ENDOMETRIUM
 CARCINOMA, EPIDEMIOLOGY, KENTUCKY (2480)
 HYPERPLASIA, ADENOCARCINOMA, SULFHYDRYL GROUPS, HUMAN (2468)
 ENVIRONMENTAL HAZARD
 AIRPLANE ENGINE SOOT, BENZO(A)PYRENE, MOUSE (2228)
 CHEMICAL CARCINOGEN, GENETIC ACTION (2168)*
 SYNTHETIC SWEETENER, CYCLAMATE, SACHARIN, CARCINOGENICITY, MAN, REVIEW (2171)*
 URBAN AREA, LUNG CANCER, EPIDEMIOLOGY (2482)
 ENZYME
 ACID PHOSPHATASE, X-IRRADIATION, ULTRAVIOLET, MOUSE ENDOCRINE GLANDS (2287)
 ADENYL CYCLASE, ADRENAL GLAND, CARCINOMA, RAT (2537)
 ADENYL CYCLASE, HEPATOMA, GROWTH RATE (2498)
 ALKALINE AND ACID NUCLEASES, N-NITROSOMORPHOLINE, RAT LIVER (2247)
 ALKALINE PHOSPHATASE, REGAN ISOZYME, CANCER PATIENTS (2567)
 ASPARTYL TRANSCARBAMYLASE, RAUSCHER LEUKEMIA VIRUS, BLOOD, MOUSE (2321)
 BENZO(A)PYRENE, HYDROXYLASE, LUNG, HAMSTER (2230)
 BETA-GLUCURONIDASE, CROTON OIL, RAT (2180)
 DNA POLYMERASE, HELA, WI38 (2561)
 DNA POLYMERASE, MURINE LEUKEMIA, VIRUS (2320)
 EXONUCLEASE, LIGASE, DNA, ROUS SARCOMA VIRUS (2368)
 HISTOCHEMISTRY, SHOPE PAPILLOMA, VIRUS, RABBIT (2381)
 INDUCERS, URETHAN CARCINOGENESIS, MICE (2255)
 IODIDE PEROXIDASE, THYROID TUMOR, RAT (2557)
 LACTATE DEHYDROGENASE, CARCINOMA, PROSTATE, HAMSTER, HUMAN (2374)
 LIVER, TRANSFER RNA, ETHIONINE (2146)
 LYSOSOMAL, MELANOMA, MOUSE (2542)

LYSOZYME, RADIATION, COBALT 60, GAMMA
 IRRADIATION (2292)
 MAMMARY CELLS, HORMONES, RAT (2470)
 METHYLASE, BRAIN TUMORS, TRNA (2523)
 METHYLASE, TRANSFER RNA, CONTROL
 (2511)
 MICROBODY, MORRIS HEPATOMA (2545)
 PATTERNS, HEPATOMA, DIFFERENT GROWTH
 RATE, MICE (2547)
 PHENYLALANYL SYNTHETASE, PHENYLALANINE
 RNA (2521)
 PROTEASE, WHOLE BODY IRRADIATION,
 RABBIT (2274)
 SERINE DEHYDRATASE, DIETHYLNITROSAMINE
 RAT (2427)
 SERINE HYDROXYMETHYL TRANSFERASE,
 LIVER, FRIEND VIRUS, MOUSE (2317)
 SURVEY, REUBER MOUSE HEPATOMAS (2549)
 THYMIDINE KINASE, HERPES SIMPLEX,
 ULTRAVIOLET (2336)
 TRNA METHYLASE, ASCITES TUMOR, MOUSE
 (2509)
 TRNA METHYLASE, 1,2-DIMETHYLHYDRAZINE,
 COLONIC TUMOR, MOUSE (2216)
 TRNA METHYLASE, MALIGNANCY (2474)
 TRNA METHYLASE, MORRIS HEPATOMAS
 (2512)
 TRYPTOPHANYL TRANSFER RNA SYNTHETASE,
 LYMPHOCYTIC LEUKEMIA, HUMAN (2510)
 TUMOR ISOENZYMES, 7,12-DIMETHYLBENZ-
 (A)ANTHRACENE, OOPHORECTOMY, RAT
 (2222)
 TYROSINASE, MELANOMA, MURINE (2541)
 TYROSINE TRANSAMINASE, CYCLOHEXIMIDE,
 PUROMYCIN, HEPATOMA (2551)
 DEMIOLOGY
 CANCER, GASTROINTESTINAL TRACT, INDIA
 (2487)
 CANCER, IRAN (2488)
 CZECHOSLOVAKIA, ORAL CAVITY (2484)
 LUNG CANCER, INDUSTRIAL ENVIRONMENT
 (2482)
 LYMPHOGRANULOMATOSIS, CHILDREN,
 BULGARIA (2483)
 MESOTHELIOMA, PLEURA, ASBESTOS (2481)
 THROCYTE
 MOUSE MAMMARY TUMOR VIRUS, DNA (2345)
 VIRUS CARRIER, FRIEND, RAUSCHER, MICE
 (2322)
 THROPOIETIN
 3-METHYLCHOLANTHRENE, SKIN TUMOR,
 MOUSE (2233)
 ROGEN
 PHOSVITIN, SERYL TRNA, METAZOAN (2475)
 ONINE
 S-ETHYL-L-CYSTEINE, CARCINOGENICITY,
 PHOSPHORYLATION, MOLECULAR STRUCTURE
 SPECIFICITY, LIVER, RAT (2192)
 TRANSFER RNA, ENZYMES, LIVER (2146)
 N-ETHYL-N'-NITRO-N-NITROSOGUANIDINE
 SKIN, MOUSE (2253)
 EYE
 ORBITAL TUMOR, EPIDEMIOLOGY, UGANDA
 (2492)
 FERRITIN
 ASBESTOS, MESOTHELIOMA, HUMAN (2257)
 HEPATOMA, RAT (2550)
 FOOD
 ADDITIVES, CARCINOGENICITY, REVIEW
 (2176)*
 FREUND ADJUVANT
 3-METHYLCHOLANTHRENE, IMMUNOLOGICAL
 PROCESSES, RAT (2232)
 RAUSCHER VIRUS, LEUKEMIA, MOUSE (2323)
 GASTROINTESTINAL TRACT
 CANCER, EPIDEMIOLOGY, INDIA (2487)
 TUMOR, CHROMOSOME (2586)*
 GENETICS
 ENVIRONMENT, CHEMICAL CARCINOGEN
 (2168)*
 MUTATION (2177)*
 NEOPLASIA, FANCONI'S ANEMIA, HUMAN
 (2534)
 PHENOTYPE, POLYOMA VIRUS (2385)
 GLUCOSE
 ENHANCED UPTAKE, PSEUDOTYPE SARCOMA
 VIRUS, HAMSTER (2354)
 GROWTH
 ASCITES TUMOR, RADIATION, RAT (2496)
 MORRIS HEPATOMA (2499)
 MORRIS HEPATOMA, STRUCTURE (2495)
 STIMULATION, FACTOR, ISOELECTRIC
 FOCUSING, HUMAN (2571)
 SV40, TRANSFORMATION, MOUSE CELLS
 (2370)
 HEMATOPOIESIS
 RADIATION, MOUSE (2277)
 HEPATOMA
 DIMETHYLAMINOAZOBENZENE, ANTIGENS,
 RAT (2423)
 DNA, GENE AMPLIFICATION, RAT (2212)
 ENZYME PATTERNS, DIFFERENT GROWTH
 RATE, MICE (2547)
 HEPATECTOMY, HYPERTROPHY, RATS (2214)
 LYMPHOCYTES, MIGRATION INHIBITING
 FACTOR, GUINEA PIG (2440)
 MORRIS, GROWTH (2499)
 MORRIS, GROWTH, STRUCTURE (2495)
 NOVIKOFF, NUCLEIC ACID SYNTHESIS, RAT
 (2544)

- NUCLEOSIDES, NUCLEOTIDES, GROWTH, RAT (2497)
 NUCLEOTIDE POOLS, NUCLEOSIDES (2497)
 REUBER H-35, FERRITIN, RAT (2550)
 REUBER MOUSE, ENZYMES (2549)
 RNA, RAT (2546)
 TRNA, PHENYLALANINE, MOUSE (2585)*
 TYROSINE TRANSAMINASE, CYCLOHEXIMIDE, PUROMYCIN (2551)
- HISTOPATHOLOGY
 TUMOR, CELLULAR POLYMORPHISM, PARA-ADENOVIRUS TYPE 7, HAMSTER (2326)
- HODGKIN'S DISEASE
 LEUKEMIA, CANDIDA ALBICANS, RESISTANCE (2461)
 PARANEOPLASTIC SYNDROME, IMMUNO-SUPPRESSION (2466)*
 UGANDA, EPIDEMIOLOGY (2493)
- HORMONE
 ADRENAL GLAND, CARCINOMA, ADENYL CYCLASE (2537)
 ESTROGEN, ENZYME ACTIVITY, MAMMARY EPITHELIAL CELLS, RAT (2470)
 PROLACTIN, 7,12-DIMETHYLBENZANTHRACENE REGRESSION, RAT (2226)
 SOMATOTROPIN, GLUCOSE EFFECT, MAMMARY GLAND CANCER, UTERINE CANCER, HUMANS (2469)
- HYBRIDIZATION
 CHROMOSOME, EHRLICH'S TUMOR, TUMORIGENICITY (2514)
 MALIGNANCY, CHROMOSOME (2554)
 POLYOMA, MOUSE, HAMSTER (2382)
 SARCOMA, FIBROBLASTS, CHROMOSOMES, MURINE (2386)
 SV40, ADENOVIRUS 2, DNA (2332)
- HYDROCORTISONE
 DNA SYNTHESIS, LIVER, RAT (2262)
 N-HYDROXY-N-ACETYL-4-AMINOBIIPHENYL LIVER, NUCLEIC ACIDS, RAT (2181)
 N-HYDROXY-2-FLUORENYLBENZENE-SULFONAMIDE ACTIVATION, RAT TISSUE (2183)
 3-HYDROXYXANTHINE
 IMMUNOSUPPRESSION, CORTISONE, RAT (2188)
- HYPERPLASIA
 ALVEOLAR NODULES, MAMMARY GLAND, PHENYLALANINE, MOUSE (2191)
- 2-IMIDAZOLIDINONE
 NITRITE, WILMS' TUMOR, RAT (2184)
- IMMUNITY
 ANTIGENS, POLYOMA VIRUS, RAT (2454)
 ANTI-LYMPHOCYTE SERUM, ROUS SARCOMA VIRUS, QUAIL (2446)
- CANCER, DEOXYCHOLATE, HUMANS, ANIMALS (2465)*
 CANCER, EXPERIMENTAL MODELS, MICE (2405)
 CARCINOMA, SARCOMA, LYMPHOCYTES, HUMAN (2418)
 CARCINOMA TRANSPLANT, LYMPHOCYTE REACTION (2433)
 FIBROSARCOMA, METASTASIS, MICE (2425)
 IMMUNOGENICITY, MAMMARY TUMOR VIRUS, MICE (2402)
 LYMPHOCYTES, MIGRATION INHIBITING FACTOR, HEPATOMA, GUINEA PIG (2440)
 MELANOMA, TUMOR-SPECIFIC, HUMAN (2438)
 POLYOMA, ROUS TUMOR, RATS (2455)
 POLYOMA TRANSFORMED BHK, HYBRIDS, SUPERINFECTION (2388)
 RADIATION, MAMMARY CARCINOMA, MICE (2416)
 SARCOMA, RNA, BENZOPYRENE, RAT (2428)
 SURVEILLANCE, 3-METHYLCHOLANTHRENE, MICE (2424)
 TRANSPLANT, LYMPHOID CELL REACTION (2408)
 TUMOR, LEUKEMIA (2159)
 TUMOR, LYMPH NODE (2462)
 TUMOR, RNA, GUINEA PIG (2464)*
 TUMOR, SPLEEN CELL, MOUSE (2459)
 TUMOR HETEROGRAFT, DIET, RAT (2401)
 X-IRRADIATION, LYMPHOMA CELLS, MOUSE (2289)
- IMMUNIZATION
 ROUS SARCOMA VIRUS, CHICKEN (2436)
- IMMUNOGLOBULIN
 ALPHA2-GLOBULIN, RADIATION, BLOOD, BONE MARROW (2278)
 ALPHA2-GLOBULIN, RADIATION, BONE MARROW, MOUSE (2276)
 CARCINOMA, MELANOMA, SARCOMA, HUMAN (2419)
 DEFICIENCY, MACROGLOBULINAEMIA, MYELOMATOSIS, HUMAN (2451)
 ISOANTIGENS, BURKITT'S LYMPHOMA, HUMAN (2158)
 LYMPHOMA, MICE (2441)
 MYELOMA, LIPIDS, MAN (2445)
 MYELOMA, PROTEIN, HUMAN (2443)
 PLASMA CELL TUMORS, TRNA, ISOACCEPTING RETICULOCYTES, MICE (2504)
 SYNTHESIS, RNA, MYELOMA, MOUSE (2450)
- IMMUNOLOGY
 ANTIGENIC VARIABILITY, POLYOMA VIRUS, MOUSE (2391)
 LEUKEMIA, CELLS, HUMAN (2406)
 LYMPHOCYTES, EPSTEIN BARR VIRUS,

ANTIGEN, DELAYED HYPERSENSITIVITY,
 HUMAN (2421)
 MAMMARY GLAND TUMOR, LEUKEMIA, MOUSE
 (2410)
 RHABDOMYOSARCOMA, CYTOTOXIC FACTOR,
 MOUSE (2432)
 SEROLOGY, RNA TUMOR VIRUS, HAMSTER
 (2395)*
 SV40, SENSITIVITY, HAMSTER (2449)
 TUMOR, FRIEND VIRUS, RAT (2411)
 TUMOR, HOST RESPONSE, COLONY FORMING
 CELLS, MICE (2404)
 VIRAL INTERFERENCE, FELINE LEUKEMIA
 COMPLEX (2311)
 IMMUNOSUPPRESSION
 HAMSTER, ROUS SARCOMA VIRUS (2360)
 HODGKIN'S DISEASE, PARANEOPLASTIC
 SYNDROME (2466)*
 3-HYDROXYXANTHINE, CORTISONE, RAT
 (2188)
 LYMPHOMA, ANTILYMPHOCYTE SERUM, MOUSE
 (2431)
 RADIATION, LANDSCHUTZ ASCITES,
 GROWTH, RAT (2496)
 INFECTIVITY
 RAUSCHER LEUKEMIA VIRUS, CELL
 PERMEATION, MOUSE (2318)
 INHIBITOR
 INTERFERON, POLY I:C, MAMMARY
 CARCINOMA, MOUSE (2346)
 INTERFERON
 POLY I:C, INHIBITOR, MAMMARY TUMOR,
 MOUSE (2346)
 TRANSFORMATION, POLYOMA, BHK (2390)
 TESTES
 METAPLASIA, EPIDEMIOLOGY, JAPAN (2489)
 W
 GRANULAR CELL AMELOBLASTOMA, ULTRA-
 STRUCTURE, HUMAN (2568)
 RYOTYPE
 DIETHYLNITROSAMINE, LIVER, SPLEEN,
 RAT (2243)
 LYMPHOMA, LANDSCHUTZ (2524)
 Spleen
 HERPES TYPE VIRUS, TUMOR, FROG (2338)
 RNA POLYMERASE, AFLATOXIN B1, MOUSE
 (2207)
 GENETICS
 CELL DEPLETION, INTESTINE, MOUSE
 (2282)
 LACTATION
 LACTOSE, 7,12-DIMETHYLBENZ(A)ANTHRA-
 CENE, MAMMARY GLAND, FIBROADENOMA,
 RAT (2223)
 LEUKEMIA

ACUTE GRANULOCYTIC, CYTOGENETICS,
 HUMAN (2582)*
 BONE MARROW, PROLIFERATION (2170)*
 C-VIRUS, GS ANTIGEN, RODENT (2457)
 CARCINOMA, COMBINED CASES (2578)*
 CELL, IMMUNOLOGY, HUMAN (2406)
 CHROMOSOMAL ABNORMALITY, REVIEW, HUMAN
 (2175)*
 CHROMOSOME, ABNORMALITY (2577)*
 CHROMOSOME, BENZENE, PANCYTOPENIA
 (2273)*
 CHRONIC LYMPHOCYTIC, RNA, HUMAN (2517)
 CHRONIC MYELOLEUKEMIA, CYTOGENETICS
 (2574)*
 DNA, 5-METHYLCYTOSINE, HUMAN (2530)
 FAMILIAL (2576)*
 FAMILY G, INCIDENCE, COLON (2533)
 FRIEND VIRUS, COMPLEMENT FIXATION,
 MOUSE (2456)
 GLYCOLIPID, LEUKOCYTE, HUMAN (2563)
 GROWTH STAGES, ANTIBODY, L1210, MICE
 (2448)
 HISTONES, INHIBITION, RNA SYNTHESIS,
 HUMAN (2515)
 HODGKIN'S DISEASE, RESISTANCE, CANDIDA
 ALBICANS (2461)
 INFECTIOUS MONONUCLEOSIS, BURKITT'S
 LYMPHOMA, CELL POPULATION (2494)
 LYMPHOCYTIC, TRYPTOPHANYL TRANSFER
 RNA SYNTHETASE, HUMAN (2510)
 LYMPHOMA, PHENYLALANINE TRANSFER RNA,
 HUMAN (2520)
 MAZURENKO VIRUS, SPECIES SPECIFICITY,
 DOG, MOUSE (2319)
 MURINE, VIRAL ANTIGENS, DETECTION
 (2413)
 MYELOBLASTIC, DNA, CHROMOSOME, HUMAN
 (2564)
 RAUSCHER VIRUS, ANTIGEN SUBUNITS,
 HEMAGGLUTINATION-INHIBITION ASSAY
 (2409)
 RAUSCHER VIRUS, FREUND ADJUVANT, MOUSE
 (2323)
 REGRESSION, VIRUS, FRIEND, MICE (2313)
 SPLENECTOMY, MOUSE (2552)
 STRONTIUM 90 RADIATION, MOUSE (2285)
 tRNA, EMBRYONIC TISSUE (2503)
 TUMORS, IMMUNITY (2159)
 VIRUS, ANTIGENICITY, HUMAN CELLS,
 ANIMAL CELLS (2295)
 VIRUS, SPREAD, BIRD (2166)*
 LEUKOCYTE
 CARCINOMA, MIGRATION INHIBITION (2452)
 CYCLOHEXYLAMINE, MUTAGENESIS, HUMAN
 (2203)

- HERPES-LIKE VIRUS, INFECTION, GUINEA PIG (2335)
LEUKEMIA, GLYCOLIPID, HUMAN (2563)
- LIPID
GLYCOLIPID, TRANSFORMED CELL, HAMSTER (2477)
SERUM, MYELOMA, IMMUNOGLOBULINS, MAN (2445)
- LIVER
2-ACETYLAMINOFLUORENE, ANTIGEN, RAT (2426)
AFLATOXIN B₁, CARCINOMA, HEPATECTOMY, RAT (2210)
2-AMINO-N-ACETYLFLUORENE, CARCINOMA, PORPHYRINS, RAT (2190)
CARCINOGENS, PROTEIN SYNTHESIS (2151)
CARCINOMA, CIRRHOSIS, AFLATOXIN, RAT (2206)
CIRRHOSIS, DIET, HEPATOCARCINOMA, RAT (2471)
CYCASIN, DIET, HUMAN (2490)
7,12-DIMETHYLBENZ(A)ANTHRACENE, DNA BINDING, RAT (2224)
7,12-DIMETHYLBENZ(A)ANTHRACENE, HEPATECTOMY, RAT (2218)
DIMETHYLNITROSAMINE, MOUSE (2246)
ENZYMES, TRANSFER RNA, ETHIONINE (2146)
HEPATOMA, CHROMATIN, RNA, RAT (2198)
N-HYDROXY-N-ACETYL-4-AMINOBIIPHENYL, NUCLEIC ACIDS, RAT (2181)
KIDNEYS, X-IRRADIATION, AUTO-RADIOGRAPHY, MICE (2279)
3-METHYL-4-DIMETHYLAMINOAZOBENZENE, BINDING, RAT (2211)
MITOCHONDRIA, MELANOMA, AMINO ACIDS, HAMSTER (2540)
MITOCHONDRIA, PHOSPHORYLATION, ETHIONINE, S-ETHYL-L-CYSTEINE, RAT (2192)
PHENOBARBITAL, 3-METHYLCHOLANTHRENE, RAT (2237)
TRANSFER RNA, MORRIS HEPATOMA, OVA (2526)
- LUNG
ADENOCARCINOMA, NITROSAMINE, MOUSE (2239)
ADENOMA, METHOTREXATE, CYCLO-PHOSPHAMIDE, MOUSE (2185)
ADENOMA, NITROSAMINE, SODIUM NITRITE, MOUSE (2241)
ADENOMA, THYMECTOMY, MICE (2430)
BENZO(A)PYRENE, UPTAKE, HAMSTER (2229)
CANCER, EPIDEMIOLOGY, URBAN AREA (2482)
- CANCER, PRECURSOR ILLNESS (2264)
CELL, CIGARETTE SMOKE, GUINEA PIG (2261)
DIETHYLNITROSAMINE, HAMSTER (2242)
DIETHYLNITROSAMINE, LIVER, MICE (2245)
DIMETHYLNITROSAMINE, MOUSE (2246)
IRRADIATION, ADENOMA, TUMOR AGENT, MOUSE (2286)
MESOTHELIOMA, ABDOMEN, ASBESTOS, FERRITIN, HUMAN (2257)
PATHOGENESIS, CANCER, TUBERCULOSIS (2472)
PULMONARY METASTASES, LYMPHANGIOSIS, PATHOGENESIS, HUMAN (2473)
- LYMPH NODE
TUMOR IMMUNITY, MOUSE (2462)
- LYMPHOCYTE
ANTILYMPHOCYTE SERUM, SARCOMA, MICE (2442)
CANCER PATIENTS, PHYTOHEMAGGLUTININ, TRANSFORMATION, ALLOGENEIC PLASMA (2460)
CARCINOMA, SARCOMA, IMMUNITY, HUMAN (2418)
DNA SYNTHESIS, LYMPHOGRANULOMA (2584)*
INDUCTION, ANTIGEN, EPSTEIN BARR VIRUS, MAN (2421)
MIGRATION INHIBITING FACTOR, HEPATOMA, GUINEA PIG (2440)
SPLEEN, TRANSPLANT, RAT (2429)
TRANSPLANTED CARCINOMA, LYMPHOID CELL REACTION (2408)
TRANSPLANTED CARCINOMA, REACTION (2433)
- LYMPHOGRANULOMATOSIS
EPIDEMIOLOGY, CHILDREN, BULGARIA (2483)
- LYMPHOMA
HERPES SAIMIRI, MARMOSET (2341)
IMMUNOGLOBULINS, MICE (2441)
LANDSCHUTZ, KARYOTYPE (2524)
LEUKEMIA, PHENYLALANINE TRANSFER RNA, HUMAN (2520)
REOVIRUS 3, MURINE (2316)
- MACROPHAGE
COLONY FORMING CELLS, TUMOR, MICE (2404)
- MAMMARY GLAND
ADENOCARCINOMA, GLUCOSE METABOLISM, ACETATE, MOUSE (2553)
CARCINOMA, IMMUNITY, RADIATION, MICE (2416)
CARCINOMA, THYROID, SIPPLE'S SYNDROME (2581)*

EPITHELIAL CELLS, ENZYME ACTIVITY,
 ESTROGEN, RAT (2470)
 FIBROADENOMA, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, LACTOSE, RAT (2223)
 HYPERPLASTIC ALVEOLAR NODULE,
 PHENYLALANINE, MOUSE (2191)
 HYPOTHALAMUS, TUMOR, MOUSE (2501)
 NEOPLASIA, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, ISOENZYMES, OOPHORECTOMY
 RAT (2222)
 TAIWAN, CANCER, EPIDEMIOLOGY (2491)
 TUMOR, FRIEND LEUKEMIA VIRUS,
 RADIATION, MOUSE (2348)
 TUMOR, KLINEFELTER'S SYNDROME, MAN
 (2566)
 TUMOR, LEUKEMIA, B PARTICLES,
 C PARTICLES, MOUSE (2410)
 TUMOR, MAST CELLS, 7,12-DIMETHYL(A)-
 ANTHRACENE, RAT (2227)
 TUMOR, MURINE TRACE ANTIGEN (2422)
 TUMOR, VIRUS, ANTIBODIES, MICE (2453)
 TUMOR, VIRUS, ANTIGEN, MURINE (2160)
 VIRUS, IMMUNOGENICITY, MICE (2402)
 MAST CELLS
 CROTON OIL, INFLAMMATION, RAT (2182)
 MELANOMA
 AMINO ACIDS, MITOCHONDRIA, LIVER,
 HAMSTER (2540)
 FISH, XIPHOPHORUS, CROSS BREEDING,
 SEX (2522)
 GROWTH, XIPHOPHORIN FISH, ALBINO
 (2559)
 HARDING-PASSEY, ULTRASTRUCTURE, MURINE
 (2543)
 LYSOSOMAL ENZYME, MOUSE (2542)
 MALIGNANT, MELANOCYTE, ULTRASTRUCTURE
 (2560)
 TUMOR-SPECIFIC IMMUNITY, HUMAN (2438)
 TYROSINASE, PROPERTIES, MURINE (2541)
 MENINGIOMA
 CHROMOSOME, HUMAN (2519)
 PHILADELPHIA CHROMOSOME, HUMAN (2532)
 MESENCHYMAL TUMORS
 SPONTANEOUS, NEWT (2555)
 MESOTHELIOMA
 ASBESTOS, OCCUPATIONAL EXPOSURE,
 EPIDEMIOLOGY (2481)
 METABOLISM
 CARBOHYDRATES, ADENOVIRUS TYPE-12, RAT
 (2333)
 CATECHOLAMINE, NEOPLASTIC TISSUE, MAN
 (2587)*
 CHOLESTEROL, MORRIS HEPATOMA (2548)
 DIBENZ(A,H)ANTHRACENE, EPOXIDE INTER-
 MEDIATE, LIVER, RAT (2221)
 GLUCOSE, ACETATE, MAMMARY ADENO-
 CARCINOMA, MOUSE (2553)
 GLUCOSE, RADIATION, MOUSE (2284)
 NOVIKOFF HEPATOMA, GLUCOSE, ADENINE
 NUCLEOTIDES, ENERGY (2539)
 PYRUVATE, X-IRRADIATION, THYMOCYTES,
 RAT (2293)
 METAL
 HEAVY IONS, CARCINOGENICITY, DIMETHYL-
 SULFOXIDE, HYDROGEN PEROXIDE (2187)
 NICKEL, REVIEW (2154)
 METAPLASIA
 INTESTINE, EPIDEMIOLOGY, JAPAN (2489)
 METASTASIS
 IMMUNE STATUS, FIBROSARCOMA, MICE
 (2425)
 PRIMARY TUMOR, DNA, HUMAN (2516)
 METHOTREXATE
 HEPATOMA, LUNG ADENOMA, CARCINOMA,
 MOUSE (2185)
 METHYL METHANE SULFONATE
 UNSCHEDULED DNA SYNTHESIS, MUSCLE, RAT
 (2201)
 METHYLATION
 EMBRYONIC TISSUE, ONCOGENIC SYSTEMS,
 TRNA, LEUKEMIA (2503)
 5-METHYLURIDINE, TRNA, ESCHERICHIA
 COLI (2508)
 MORRIS HEPATOMAS, TRANSFER RNA (2512)
 RNA METHYLASE, ENZYMES, MALIGNANCY
 (2474)
 TRNA, DIFFERENTIATION, NEOPLASIA,
 REVIEW (2147)
 TRNA, MAMMARY TUMOR, MOUSE (2506)
 TRNA, NEOPLASTIC CELLS (2507)
 METHYLBUTYLNITROSAMINE
 NOSE, CARCINOMA, RAT (2265)*
 3-METHYLCHOLANTHRENE
 BACILLUS CALMETTE-GUERIN, MOUSE
 (2272)*
 ERYTHROPOIETIN, SKIN TUMOR, MOUSE
 (2233)
 FREUND ADJUVANT, IMMUNOLOGY, RAT
 (2232)
 IMMUNOLOGICAL SURVEILLANCE, MICE
 (2424)
 MUCOUS LUBRICATION, CERVIX, MOUSE
 (2235)
 PHENOBARBITAL, LIVER, RAT (2237)
 POLYADENYLIC-POLYURIDYLIC ACID,
 SARCOMA, MICE (2403)
 SARCOMA, RESPONSIVENESS, PHYTO-
 HEMAGGLUTININ, MICE (2435)
 SKIN MORPHOLOGY, MOUSE (2189)
 SKIN TUMOR, EFFECT OF VITAMIN B12,

- MOUSE (2234)
TUMOR, BCG VACCINE, LIVER, SPLEEN,
RAT (2238)
TUMOR, CHROMOSOME, HAMSTER (2236)
3'-METHYL-4-DIMETHYLAMINOAZOBENZENE
BILE ACID, RAT (2213)
LIVER, BINDING, RAT (2211)
N-METHYL-N'-NITRO-N-NITROSOGUANIDINE
MITOSIS, HAMSTER CELLS (2250)
SKIN, MOUSE (2253)
VAGOTOMY, SPLANCHNICOTOMY, STOMACH
TUMOR, RAT (2251)
METHYL-NITROSOBIURET
CANCER, STOMACH, RAT (2252)
N-METHYL-N-NITROSO-B-D-GLUCOSYLAMINE
GALACTOSYLAMINE, ANALOGUE,
CARCINOGENICITY, RAT (2244)
N-METHYL-N-NITROSUREA
TISSUE DISTRIBUTION, RAT (2249)
MICROBODY
MORRIS HEPATOMA, ENZYME (2545)
MIGRATION
LEUKOCYTES, CARCINOMA EXTRACTS,
INHIBITION (2452)
LYMPHOMA CELL (2314)
MITOCHONDRIA
MELANOMA, LIVER, AMINO ACIDS, HAMSTER
(2540)
PHOSPHORYLATION, ETHIONINE,
S-ETHYL-L-CYSTEINE, LIVER, RAT
(2192)
RIBOSOMES, HELA CELLS (2528)
MITOSIS
N-METHYL-N'-NITRO-N-NITROSOGUANIDINE,
HAMSTER CELLS (2250)
MUTAGENESIS
AFLATOXIN B1, DROSOPHILA (2208)
CYCLOHEXYLAMINE, LEUKOCYTES (2203)
MUTATION
ADENOVIRUS 5, TEMPERATURE SENSITIVITY,
5-BROMODEOXYURIDINE (2327)
FROG VIRUS, TEMPERATURE SENSITIVITY
(2301)
GENETICS (2177)*
GENETICS, CARCINOMA, PHACOMATOSES
(2583)*
MYELOMA
ANTIBODIES, MOUSE TISSUE (2414)
IMMUNOGLOBULIN, LIPIDS, SERUM, MAN
(2445)
IMMUNOGLOBULIN SYNTHESIS, RNA, MOUSE
(2450)
PROTEIN, HAPTEN BINDING, MOUSE
(2444)
PROTEIN, STRUCTURE, HUMAN (2443)
SPOUSE (2535)
SURFACE ANTIGEN, MOUSE (2415)
NASOPHARYNX
CARCINOMA, REVIEW (2162)
VIRUS, EPSTEIN BARR VIRUS, CARCINOMA
(2463)*
NEOPLASIA
GENETICS, FANCONI'S ANEMIA, HUMAN
(2534)
NERVOUS SYSTEM
TUMORS, ISRAEL, EPIDEMIOLOGY (2485)
NICKEL
BLOOD, URINE, EXCRETION, RAT (2268)*
HAMSTER (2195)
REVIEW (2154)
NICOTINAMIDE
PANCREAS, TUMOR, RAT (2186)
4-NITROQUINOLINE-1-OXIDE
KIDNEY, RAT (2270)*
NITROSAMINE
ADENOCARCINOMA, LUNG, MOUSE (2239)
SODIUM NITRITE, LUNG, ADENOMA, MOUSE
(2241)
SUSCEPTIBILITY, GUINEA PIG (2152)
N-NITROSOMORPHOLINE
DIMETHYLNITROSAMINE, SERINE
DEHYDRATASE, RAT (2427)
NUCLEASES, LIVER, RAT (2247)
N-(BETA-CHLOROETHYL)-N-NITROSURETHAN
TUMOR, STOMACH, LUNG, RAT (2256)
NOSE
METHYLBUTYLNITROSAMINE, CARCINOMA, RAT
(2265)*
NUCLEIC ACID
LIVER, N-HYDROXY-N-ACETYL-4-AMINO-
BIPHENYL, RAT (2181)
RNA, DNA, METHYLASES (2150)
ROUS VIRUS, REPLICATION, CHICK EMBRYO
CELLS (2362)
SYNTHESIS, HEPATOMA, RAT (2544)
NUCLEOTIDE
ADENINE, ENERGY, GLUCOSE, NOVIKOFF
HEPATOMA (2539)
NUCLEOSIDES, HEPATOMA, GROWTH, RAT
(2497)
OCCUPATIONAL HAZARD
ASBESTOS, MESOTHELIOMA, EPIDEMIOLOGY
(2481)
BENZENE, TOLUENE, CHROMOSOME CHANGES
(2193)
BENZO(A)PYRENE, ALUMINIUM PLANT (2259)
OIL
OVERHEATED, CARCINOGENICITY,
BENZO(A)PYRENE, RAT (2196)
ORAL CAVITY

FACE, TUMORS, EPIDEMIOLOGY,
 CZECHOSLOVAKIA (2484)
 RAL CONTRACEPTIVE
 CERVICAL HYPERPLASIA (2478)*
 STEOSARCOMA
 FELINE SARCOMA VIRUS, TRANSFORMATION,
 HUMAN (2298)
 ULTRASTRUCTURE, TUBULAR STRUCTURES
 (2565)
 VARY
 NEOPLASIA, DNA, CHROMOSOME, HUMAN
 (2536)
 ANCREAS
 CANCER EPIDEMIOLOGY, NEGRO (2479)
 TUMOR, NICOTINAMIDE, STREPTOZOTOCIN,
 RAT (2186)
 ATHOGENESIS
 HORMONE-PRODUCING TUMOR, ADRENAL
 CORTEX, REVIEW (2161)
 NEOPLASIA, PULMONARY TUBERCULOSIS
 (2472)
 PULMONARY LYMPHANGIOSIS, METASTASIS,
 HUMAN (2473)
 ATHOLOGY
 TUMOR, MALIGNANT, MORPHOLOGY (2165)*
 HACOMATOSES
 MUTATION, GENETICS (2583)*
 HENOBARBITAL
 LIVER, 3-METHYLCHOLANTHRENE, RAT
 (2237)
 HYTOHEMAGGLUTININ
 LYMPHOCYTE, CANCER PATIENTS,
 ALLOGENEIC PLASMA (2460)
 LACENTA
 BENZO(A)PYRENE, KIDNEY, MOUSE (2231)
 POLLUTION
 BENZO(A)PYRENE, FIBROSARCOMA, MOUSE
 (2258)
 POLYCYCLIC HYDROCARBONS
 CELL TRANSFORMATIONS, HAMSTER (2197)
 POLYCYCLIC THIAZOLE
 CARCINOGENS (2269)*
 POLYCYTHEMIA
 CHROMOSOME ABERRATIONS, HUMAN (2531)
 POLYINOSINIC-POLYCYTIDYLIC ACID
 LYMPHOMA, THYMUS, 7,12-DIMETHYLBENZ-
 (A)ANTHRACENE, MOUSE (2225)
 POLYNUCLEOTIDE
 POLYADENYLIC-POLYURIDYLIC ACID,
 3-METHYLCHOLANTHRENE, SARCOMA, MICE
 (2403)
 POLYPS
 CARCINOMA, STOMACH (2569)
 POLYRIBOSOME
 CYTOPLASMIS, PROTEIN SYNTHESIS,

EHRLICH'S TUMOR (2529)
 PRECANCEROUS CONDITION
 CERVIX, CHROMOSOME, HUMAN (2467)
 PROLIFERATION
 BONE MARROW, LEUKEMIA (2170)*
 PROPANE SULTONE
 CARINOGENNICITY, PROPYLENE IMINE, RAT
 (2263)
 PROPYLENE IMINE
 CARCINOGENICITY, PROPANE SULTONE, RAT
 (2263)
 PROSTATE
 CARCINOMA, LACTATE DEHYDROGENASE,
 HAMSTER, HUMAN (2374)
 CARCINOMA, TESTICLE, HUMAN (2572)
 VIRUS, VENEREAL DISEASE, CIRCUMCISION
 (2394)*
 PROTEIN
 RIBONUCLEOPROTEIN SYNTHESIS,
 MITOCHONDRIA, HELA CELL (2570)
 RIBOSOMAL, SYNTHESIS, EHRLICH'S TUMOR
 (2529)
 SULFHYDRYL GROUPS, ENDOMETRIUM,
 ADENOCARCINOMA, HUMAN (2468)
 SYNTHESIS, LIVER, CARCINOGENS (2151)
 VIRUS, ADENOVIRUS 5, ARGININE, HUMAN
 CELLS (2328)
 RADIATION
 ALPHA2-GLOBULIN, BLOOD, BONE MARROW,
 CELL POPULATION (2278)
 BONE MARROW, ALPHA2-GLOBULIN, MOUSE
 (2276)
 COBALT 60, GAMMA IRRADIATION, LYSOZYME
 ENZYME (2292)
 HEMATOPOIESIS, MOUSE (2277)
 IMMUNITY, MAMMARY CARCINOMA, MICE
 (2416)
 INTESTINE, CELL DEPLETION KINETICS,
 MOUSE (2282)
 LEUKEMOGENESIS, VIRUS, HOST FACTORS,
 MICE (2434)
 RARE EARTH METALS, 7,12-DIMETHYLBENZ-
 (A)ANTHRACENE, 1,2,5,6-DIBENZANTHRA-
 CENE, RAT (2294)*
 STRONTIUM 90, IODINE 131, RESPIRATORY
 PATTERN, MOUSE (2284)
 STRONTIUM 90, LEUKEMIA, MOUSE (2285)
 SUNLIGHT, SQUAMOUS CELL CARCINOMA,
 CAT (2288)
 TRANSPLANTATION, LUNG, ADENOMA, MOUSE
 (2286)
 X-IRRADIATION, CHROMOSOME ABERRATIONS,
 RABBIT, HUMAN (2280)
 X-IRRADIATION, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, SKIN PAPILLOMA, MOUSE

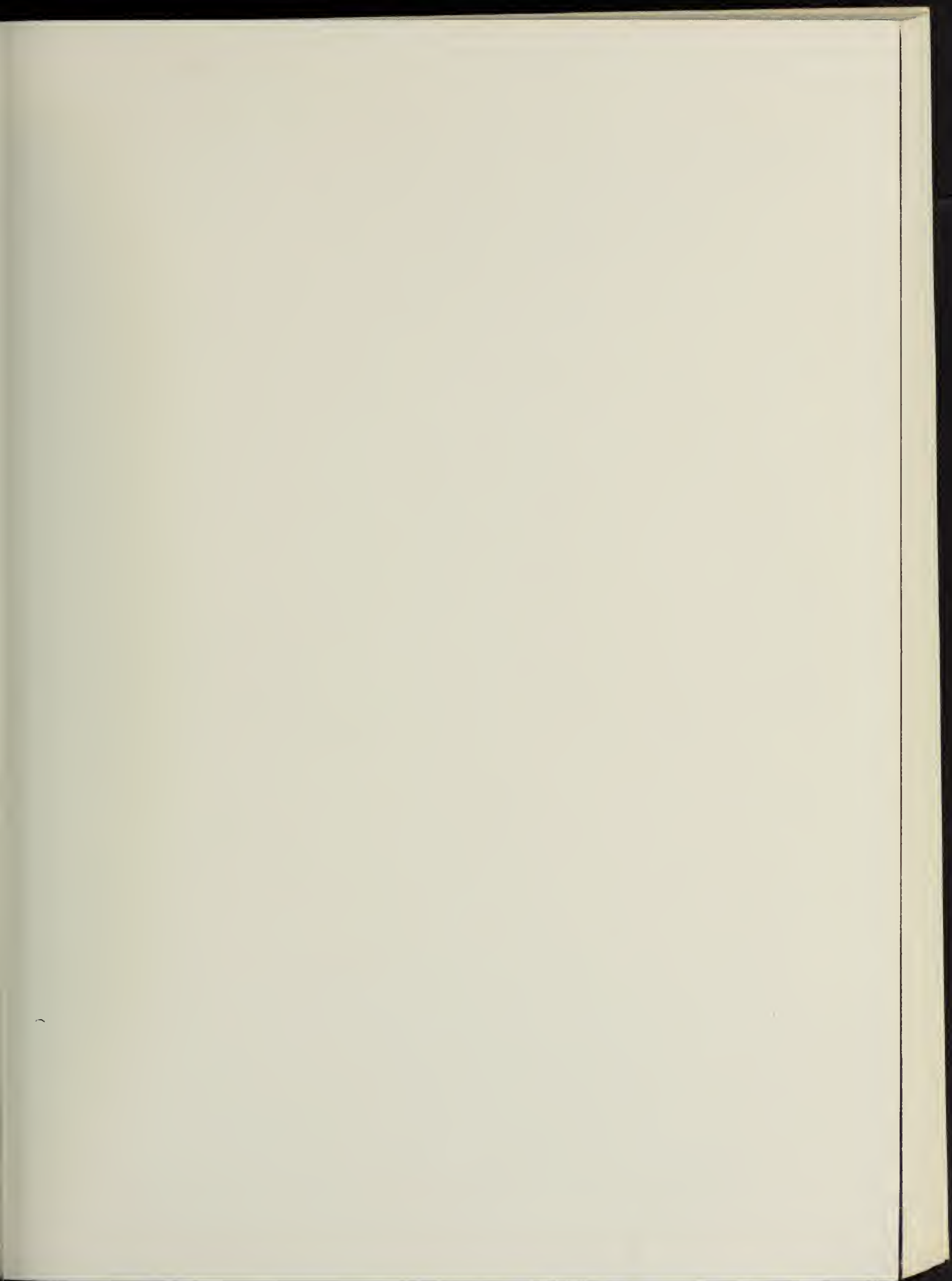
- (2219)
X-IRRADIATION, IODINE 131, THYROID,
CHROMOSOME DAMAGE, HUMAN (2283)
X-IRRADIATION, LIVER, KIDNEY, MOUSE
(2279)
X-IRRADIATION, LYMPHOMA, RESISTANCE,
MOUSE (2289)
X-IRRADIATION, NUCLEIC ACID SYNTHESIS,
HAMSTER CELLS (2290)
X-IRRADIATION, PYRUVATE, THYMOCYTES,
RAT (2293)
X-IRRADIATION, SPERMATOZOA, DOMINANT
LETHALITY, MOUSE, RAT (2281)
X-IRRADIATION, SPLEEN, BONE MARROW,
REGENERATION, MOUSE (2275)
X-IRRADIATION, ULTRAVIOLET, ACID
PHOSPHATASE, MOUSE ENDOCRINE GLANDS
(2287)
X-IRRADIATION, WHOLE BODY, PROTEASE
ACTIVITY, RABBIT (2274)
REGENERATION
X-IRRADIATION, SPLEEN, THYMUS, BONE
MARROW, MOUSE (2275)
RESISTANCE
FRIEND VIRUS, LEUKEMIA, REGRESSION,
MOUSE (2412)
RHABDOMYOSARCOMA
CHROMOSOME, DOUBLE-MINUTE, HUMAN
(2525)
RIBOSOME
MITOCHONDRIA, HELA CELLS (2528)
RNA
ANTIBIOTICS, EXORIBONUCLEASE, EHRlich
ASCITES TUMOR (2179)
CHROMATIN, LIVER, HEPATOMA, RAT (2198)
CHRONIC LYMPHOCYTIC LEUKEMIA, HUMAN
(2517)
DNA, NUCLEIC ACID METHYLASES (2150)
HISTONES, INHIBITION, LEUKEMIA, HUMAN
(2515)
KIDNEY, AFLATOXIN B1, MOUSE (2207)
LIVER, HEPATOMA, RAT (2546)
• METHYLATING ENZYMES, VIRUS, E. COLI
(2304)
MURINE SARCOMA, VIRUS SPECIFIC (2355)
MURINE VIRUSES, HOST RANGE ALTERATION,
HUMAN CELL CULTURES (2352)
PHENYLALANINE TRANSFER, LEUKEMIA,
LYMPHOMA, HUMAN (2520)
PHENYLALANINE TRANSFER SYNTHETASE,
(2521)
SARCOMA, BENZOPYRENE, IMMUNITY, RAT
(2428)
SARCOMA, ROUS VIRUS, CHICKEN, MOUSE
(2365)
SERYL TRNA, ESTROGEN, PHOSVITIN,
ROOSTER (2475)
SYNTHESIS, AFLATOXIN B1, HEPATECTOMY,
LIVER, RAT (2205)
SYNTHESIS, INFECTION, ADENOVIRUS 12,
HAMSTER (2329)
SYNTHESIS, POLYOMA VIRUS, MOUSE
(2400)*
TRANSFER, N-ACETOXY-2-ACETYLAMINO-
FLUORENE (2199)
TRANSFER, BRAIN TUMOR, BASE COMPOSI-
TION (2527)
TRANSFER, ESCHERICHIA COLI, 5-METHYL-
URIDINE (2508)
TRANSFER, ESCHERICHIA COLI, MUTATION
(2148)
TRANSFER, ISOACCEPTING, RETICULOCYTES,
PLASMA CELL TUMORS, MICE (2504)
TRANSFER, LEUKEMIA, EMBRYONIC TISSUE
(2503)
TRANSFER, MAMMALIAN TISSUE, SPECIFICITY
(2505)
TRANSFER, METHYLASE, BRAIN TUMORS,
HUMAN (2523)
TRANSFER, METHYLASE, CONTROL (2511)
TRANSFER, METHYLASE, MORRIS HEPATOMA
(2512)
TRANSFER, METHYLATION, ASCITES TUMOR,
MOUSE (2509)
TRANSFER, METHYLATION, MAREK'S DISEASE
VIRUS (2309)
TRANSFER, METHYLATION, NEOPLASIA,
REVIEW (2147)
TRANSFER, METHYLATION, NEOPLASTIC
CELLS (2507)
TRANSFER, MODIFIED BASES, E. COLI
(2518)
TRANSFER, MORRIS HEPATOMA, LIVER, OVA
(2526)
TRANSFER, PHENYLALANINE, HEPATOMA,
MOUSE (2585)*
TRANSFER, SYNTHESIS, BACTERIOPHAGE,
E. COLI (2513)
TRNA GUANINE 7-METHYLASE, MAMMARY
TUMOR, MOUSE (2506)
TUMOR, IMMUNITY, GUINEA PIG (2464)*
SALIVARY GLAND
TUMOR, MYOEPITHELIAL CELL (2163)
SARCOMA
ROUS VIRUS, CARR-ZILBER STRAIN, MOUSE,
CHICK EMBRYO (2367)
SERUM
ANTIGENS, LYMPHOID TUMOR, CHICKEN
(2439)
SEX

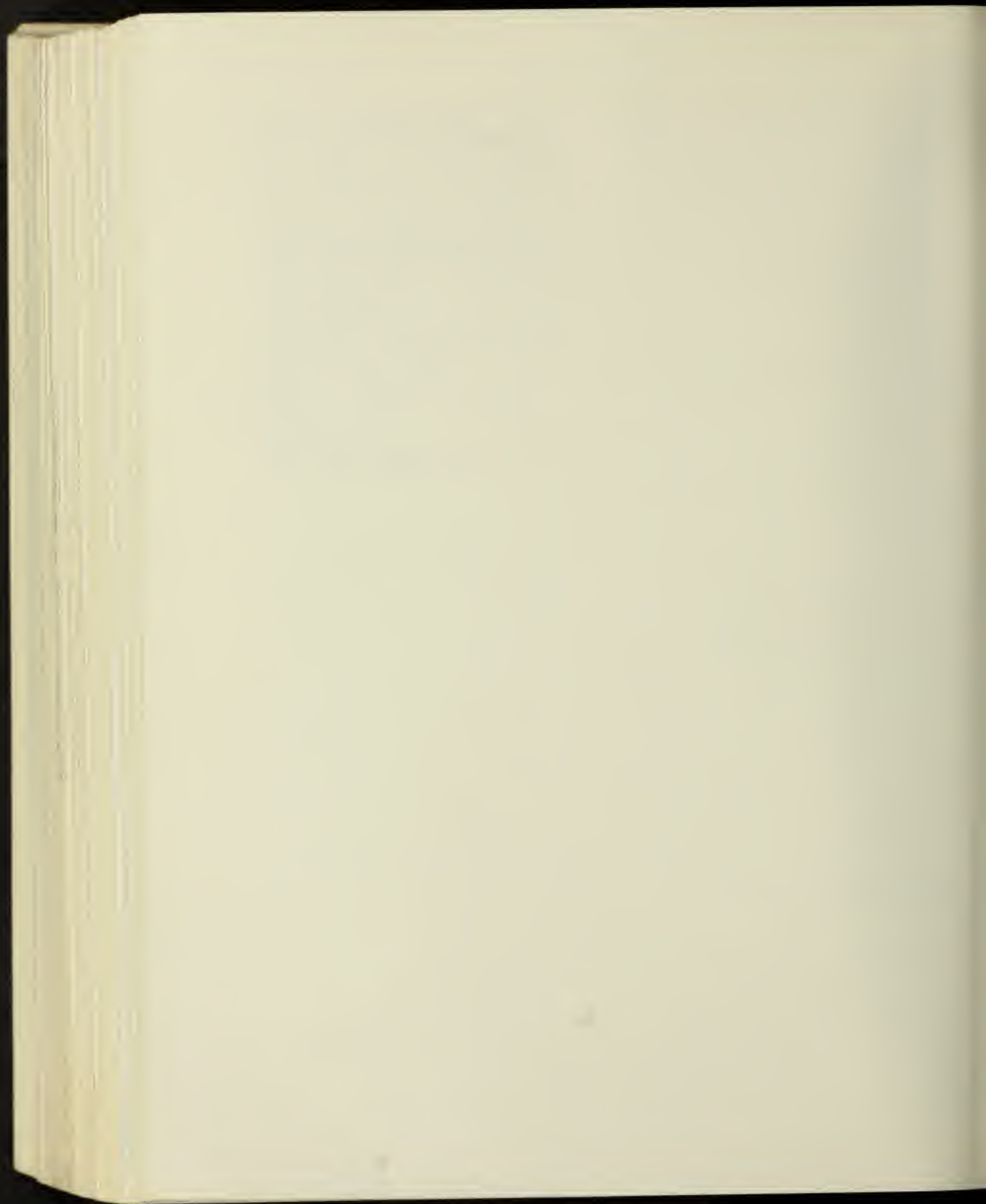
FISH, XIPHOPHORUS, CROSS BREEDING,
 MELANOMA (2522)
 SIPPLE'S SYNDROME
 THYROID, BREAST, CARCINOMA (2581)*
 SKIN
 LUNG, BONES, VINYL CHLORIDE, RAT
 (2200)
 MORPHOLOGY, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, 3-METHYLCHOLANTHRENE,
 MOUSE (2189)
 SUNLIGHT, SQUAMOUS CELL CARCINOMA,
 CAT (2288)
 TRANSFORMATION, SWEAT GLAND, TUMOR
 (2575)*
 TUMOR, 7,12-DIMETHYLBENZ(A)ANTHRACENE,
 X-RAY IRRADIATION, MOUSE (2219)
 TUMOR, ERYTHROPOIETIN, 3-METHYL-
 CHOLANTHRENE (2233)
 TUMOR, 3-METHYLCHOLANTHRENE, VITAMIN
 B12, MOUSE (2234)
 SPLEEN
 ADOPTIVE TRANSFER, IMMUNITY, MICE
 (2459)
 LEUKEMIA, MOUSE (2552)
 LYMPHOCYTES, TUMOR (2429)
 STOMACH
 N-METHYL-N'-NITRO-N-NITROSOGUANIDINE,
 VAGOTOMY, SPLANCHNICOTOMY, TUMOR,
 RAT (2251)
 METHYL-NITROSOBIURET, CANCER, RAT
 (2252)
 N-(BETA-CHLOROETHYL)-N-NITROSOURETHAN,
 LUNG, TUMOR, RAT (2256)
 POLYPS, CARCINOMA (2569)
 STREPTOZOTOCIN
 PANCREAS, TUMOR, RAT (2186)
 STRESS
 ADRENAL LESIONS, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, RAT (2217)
 SUSCEPTIBILITY
 NITROSAMINE, GUINEA PIG (2152)
 TEMPERATURE
 FROG, VIRUS, HERPES, LUCKE ADENO-
 CARCINOMA (2340)
 TESTES
 DIMETHYLNITROSAMINE, RAT (2240)
 GERMINATIVE (2573)*
 TESTICLE
 PROSTATE, CARCINOMA, HUMAN (2572)
 THYMUS
 SPLEEN, MAMMARY TUMOR, MOUSE (2344)
 SPONTANEOUS LUNG TUMOR, IMMUNITY, MICE
 (2430)
 THYROID
 BREAST, CARCINOMA, SIPPLE'S SYNDROME
 (2581)*
 CARCINOMA, JAPANESE, HAWAII, INCIDENCE
 (2486)
 PAPILLARY FOLLICULAR TUMOR, IMPLANTS,
 DIFFERENTIATION, RAT (2562)
 TUMORS, CYTOGENETICS, ENZYME, RAT
 (2557)
 TOBACCO
 CIGARETTE SMOKE, PULMONARY CELLS,
 GUINEA PIG (2261)
 COCARCINOGEN, BENZO(A)PYRENE, SKIN,
 MOUSE (2204)
 SMOKE CONDENSATE, TUMORIGENESIS,
 PROMOTION (2260)
 TRANS-4-DIMETHYLAMINOSTILBENE
 DISTRIBUTION, RAT (2271)*
 TRANSFORMATION
 AVIAN ROUS SARCOMA VIRUS, FUJINAMI
 SARCOMA VIRUS, RAT EMBRYO, IN VITRO
 (2363)
 EFFICIENCY, SV40, RAUSCHER, RAT
 (2376)
 HUMAN CELL CULTURE, KIRSTEN MURINE
 SARCOMA VIRUS, RAUSCHER MURINE
 LEUKEMIA VIRUS, HOST RANGE ALTERA-
 TIONS (2352)
 IN VITRO, NON-ONCOGENIC DEFECTIVE
 SV-40, HAMSTER (2372)
 POLYCYCLIC HYDROCARBONS, HAMSTER
 CELLS (2197)
 POLYOMA VIRUS, FIBROBLAST SUSPENSIONS,
 SURFACE INTERACTIONS (2387)
 REVERSION, VIRUS (2155)
 VIRUS, ROUS SARCOMA, GLYCOLIPID (2359)
 TRANSPLANTATION
 ADENOVIRUS 12, SV40, TUMOR, HAMSTER
 (2331)
 TUMOR, ENHANCEMENT, LYMPHOCYTES,
 SPLEEN, RAT (2429)
 TRITIUM
 DNA MOLECULAR WEIGHT, LYMPHOMA, MOUSE
 (2291)
 TUMOR
 SPONTANEOUS, MOUSE (2502)
 ULTRASTRUCTURE, MOUSE (2500)
 ULTRASTRUCTURE
 SALIVARY GLAND TUMOR, MYOEPIHELIAL
 CELLS (2163)
 TUMOR CELL, MOUSE (2500)
 URETHAN
 ENZYME INDUCER, LUNG, MOUSE (2255)
 UTERUS
 MAMMARY GLAND CANCER, SOMATOTROPIN,
 GLUCOSE EFFECT, HUMANS (2469)
 VINYL CHLORIDE

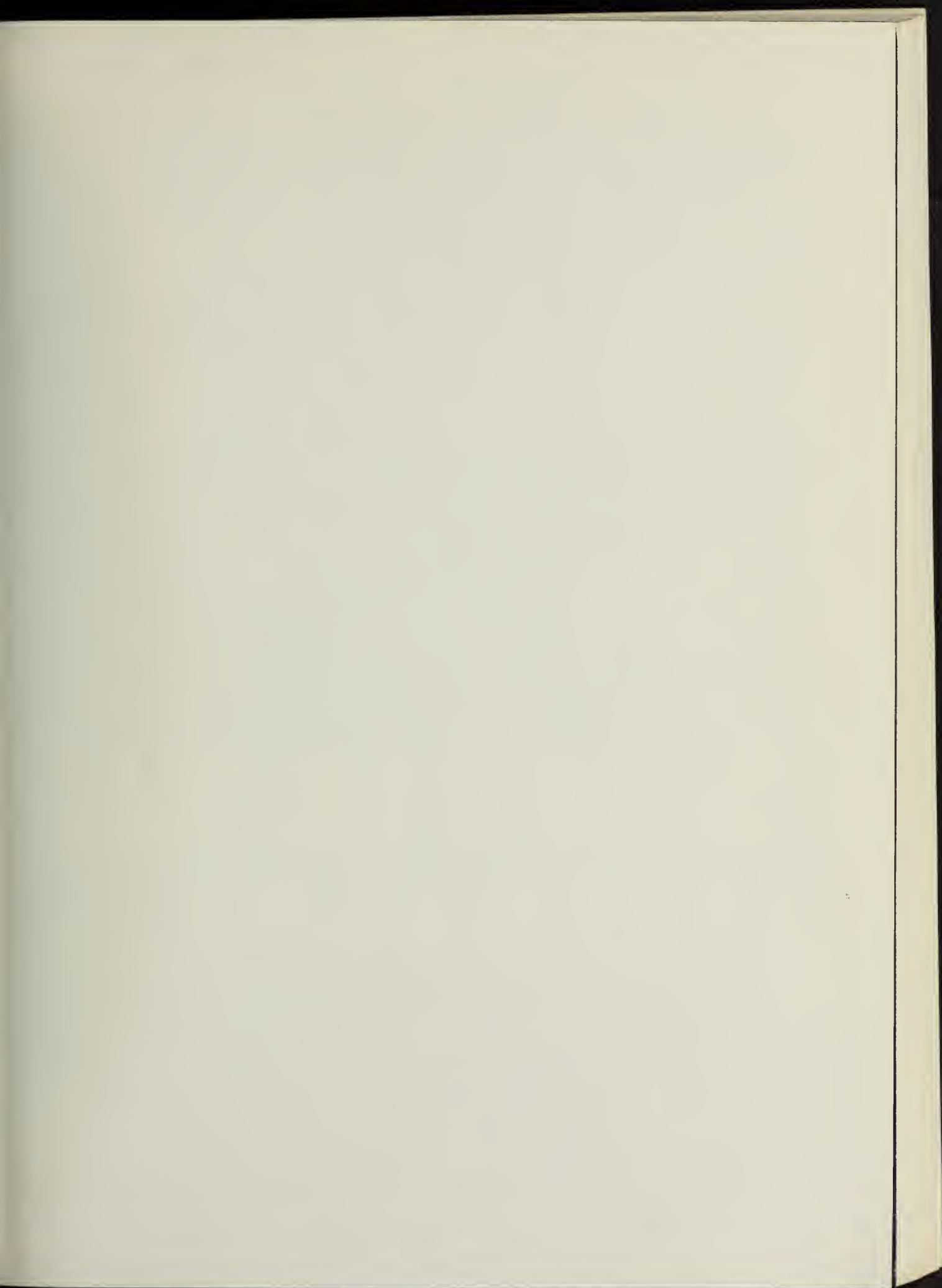
- SKIN, LUNG, TUMOR, RAT (2200)
- VIRUS
- ADENOVIRUS TYPE, COCULTIVATION (2397)*
- ADENOVIRUS 2, SV40, HYBRIDIZATION, DNA (2371)
- ADENOVIRUS 2, ULTRASTRUCTURE, INFECTED CELL (2330)
- ADENOVIRUS 5, ARGININE, PROTEIN, HUMAN CELLS (2328)
- ADENOVIRUS 5, TEMPERATURE-SENSITIVITY, MUTATION, 5-BROMODEOXYURIDINE (2327)
- PARA-ADENOVIRUS 7, TUMOR CELL POLYMORPHISM, IMMUNOLOGY, HAMSTER (2326)
- ADENOVIRUS 12, CARBOHYDRATE METABOLISM RAT (2333)
- ADENOVIRUS 12, DNA SIZES (2325)
- ADENOVIRUS 12, RNA SYNTHESIS, INFECTION, HAMSTER (2329)
- ADENOVIRUS 12, SV40, TRANSPLANTATION, TUMOR ANTIGEN, HAMSTER (2331)
- ANAL WART, CARCINOMA IN SITU (2396)*
- AVIAN LEUKEMIA, SPREAD, BIRD (2166)*
- AVIAN MYELOBLASTOSIS, OLIGOMER, MITOCHONDRIA, DNA (2308)
- AVIAN SARCOMA, ROUS, FUJINAMI, RAT EMBRYO CELLS, IN VITRO (2363)
- B AND C PARTICLES, MAMMARY GLAND CANCER, LEUKEMIA, IMMUNOLOGY, MOUSE (2410)
- C-TYPE, GS ANTIGEN, LEUKEMIA, RODENT (2457)
- C-TYPE, MAMMALIAN, ANTIGENIC SPECIFICITY (2407)
- CHICK EMBRYO LETHAL ORPHAN, ANTIGENICITY (2303)
- CIRCUMCISION, VENEREAL DISEASE, PROSTATE (2394)*
- CYTOMEGALO, PARAGANGLIOMA, HUMAN (2302)
- EPSTEIN BARR, ANTIBODY, CARCINOMA, NASOPHARYNX (2463)*
- EPSTEIN BARR, CHROMOSOME, ABERRATION (2307)
- EPSTEIN BARR, LYMPHOCYTE INDUCTION, MAN (2421)
- FELINE LEUKEMIA, ANTIGEN, ISOLATION (2312)
- FELINE LEUKEMIA, INTERFERENCE, FELINE CELLS (2311)
- FELINE SARCOMA, OSTEOSARCOMA, TRANSFORMATION, HUMAN (2298)
- FRIEND, GRAFFI, LIVER, SERINE HYDROXY-METHYL TRANSFERASE, MOUSE (2317)
- FRIEND, IMMUNOLOGY, RAT (2411)
- FRIEND, LEUKEMIA, COMPLEMENT FIXATION, MOUSE (2456)
- FRIEND, LEUKEMIA, RADIATION, MAMMARY TUMOR, MOUSE (2348)
- FRIEND, LEUKEMIA, REGRESSION, MICE (2313)
- FRIEND, LEUKEMIA, REGRESSION, RESISTANCE, MOUSE (2412)
- FRIEND, RAUSCHER, ERYTHROCYTE, CARRIER (2322)
- FROG, MUTATION, TEMPERATURE-SENSITIVITY (2301)
- GENOME, TRANSFORMATION, DNA (2156)
- HERPES, ANTIGEN, BURKITT'S LYMPHOMA, MAN (2343)
- HERPES, LUCKE ADENOCARCINOMA, FROG, TEMPERATURE (2340)
- HERPES SAIMIRI, LYMPHOMA, MARMOSSET (2341)
- HERPES SIMPLEX, ANTIBODY, PERSISTENCE, EARLE'S L CELLS, HUMAN (2334)
- HERPES SIMPLEX, CHROMOSOME, ABNORMALITY (2342)
- HERPES SIMPLEX, CYTOSINE ARABINOSIDE, CHROMOSOME CHANGES, HUMAN (2339)
- HERPES SIMPLEX, DNA SYNTHESIS, KB CELLS (2337)
- HERPES SIMPLEX, THYMIDINE KINASE, ULTRAVIOLET (2336)
- HERPES TYPE, INFECTION, LEUKOCYTE, GUINEA PIG (2335)
- HERPES TYPE, KIDNEY TUMOR, FROG (2338)
- HERPESVIRUS HOMINIS, BURKITT'S LYMPHOMA, INHIBITION (2306)
- KILHAM RAT, DNA (2399)*
- KILHAM RAT, DNA POLYMERASE (2300)
- KIRSTEN MURINE SARCOMA, RAUSCHER MURINE LEUKEMIA, GENETIC ALTERATION, HUMAN CELL CULTURE (2352)
- LEUKEMIA, ACTIVATION, SPECIES SPECIFICITY, DOG MOUSE (2319)
- LEUKEMIA, ANTIGENICITY, HUMAN CELLS, ANIMAL CELLS (2295)
- LEUKEMIA, ANTIGENS, DETECTION (2413)
- MAMMARY TUMOR, ANTIBODIES, MICE (2453)
- MAMMARY TUMOR, ANTIGEN, MURINE (2160)
- MAMMARY TUMOR, ANTIGENICITY, MICE (2349)
- MAMMARY TUMOR, ERYTHROCYTES, DNA, MOUSE (2345)
- MAMMARY TUMOR, IMMUNOGENICITY, MICE (2402)
- MAMMARY TUMOR, THYMECTOMY, SPLENECTOMY (2344)
- MAREK'S DISEASE, DNA (2310)

MAREK'S DISEASE, RNA, TRANSFER,
 METHYLATION (2309)
 MOLONEY MURINE SARCOMA, HELPER,
 ISOLATION, RAT (2353)
 MURINE LEUKEMIA, CELL FUSION (2315)
 MURINE LEUKEMIA, DNA POLYMERASE,
 MURINE CELL (2320)
 MURINE SARCOMA, DIETHYLAMINOETHYL-
 DEXTRAN, TUMOR ENHANCEMENT (2351)
 MURINE SARCOMA, MOUSE, HAMSTER, CAT,
 ANTIGEN (2356)
 MURINE SARCOMA, REVIEW (2169)*
 MURINE SARCOMA, RNA (2355)
 MURINE SARCOMA, VIRAL ANTIGENICITY,
 (2458)
 ONCOGENIC, ANIMAL CELLS, TRANSFORMA-
 TION (2164)*
 PARAMYXOVIRUS, SARCOMA, HUMAN, ULTRA-
 STRUCTURE (2558)
 PARTICLE, ANTIGEN, MAMMARY TUMOR,
 MOUSE (2347)
 POLYOMA, CELL PROLIFERATION, MURINE
 (2389)
 POLYOMA, 7,12-DIMETHYLBENZ(A)ANTHRA-
 CENE, 3-METHYLCHOLANTHRENE, CELL
 GROWTH, IN VITRO, HAMSTER (2194)
 POLYOMA, FIBROBLAST SUSPENSION,
 SURFACE INTERACTIONS (2387)
 POLYOMA, HYBRIDIZATION, MOUSE, HAMSTER
 (2382)
 POLYOMA, IMMUNITY, ANTIGENS, RAT
 (2454)
 POLYOMA, IMMUNITY, BACTERIOPHAGE, BHK
 (2388)
 POLYOMA, MUTANT, TEMPERATURE
 SENSITIVITY, DNA SYNTHESIS (2384)
 POLYOMA, PHENOTYPE (2385)
 POLYOMA, RECOVERY, METHODOLOGY (2392)*
 POLYOMA, RNA SYNTHESIS, MOUSE (2400)*
 POLYOMA, ROUS TUMOR, IMMUNITY, RAT
 (2455)
 POLYOMA, TRANSFORMATION, INTERFERON,
 BHK (2390)
 POLYOMA, TRANSFORMED CELL, TUMOR,
 HAMSTER (2383)
 POLYOMA, TUMOR CELL CLONES, ANTIGENS,
 MOUSE (2391)
 POLYOMA TUMORS, ANTIGEN, SHEEP
 ERYTHROCYTES, HAMSTER CELLS (2437)
 PSEUDOTYPE SARCOMA, HAMSTER, GLUCOSE
 UPTAKE (2354)
 RADIATION LEUKEMIA, HOST FACTORS,
 MICE (2434)
 RAUSCHER, ANTIGEN SUBUNITS,
 HEMAGGLUTINATION-INHIBITION ASSAY
 (2409)
 RAUSCHER, FREUND ADJUVANT, MOUSE
 (2323)
 RAUSCHER LEUKEMIA, ASPARTYL TRANS-
 CARBAMYLASE, BLOOD, MOUSE (2321)
 RAUSCHER LEUKEMIA, ENTRY INTO CELL,
 MOUSE (2318)
 REOVIRUS 3, LYMPHOMA, MURINE (2316)
 RNA, DNA (2299)
 RNA-METHYLATING ENZYMES, E.COLI (2304)
 RNA TUMOR VIRUS, SEROLOGY, HAMSTER
 (2395)*
 ROUS, MURINE SARCOMA, CHICK EMBRYO,
 MOUSE (2367)
 ROUS SARCOMA, ANTI-LYMPHOCYTE SERUM,
 QUAIL (2446)
 ROUS SARCOMA, DEFECTIVE, DNA POLY-
 MERASE (2398)*
 ROUS SARCOMA, DNA, EXONUCLEASE, LIGASE
 (2368)
 ROUS SARCOMA, DNA POLYMERASE, CHICKEN
 CELL (2358)
 ROUS SARCOMA, DNA SYNTHESIS, IN VITRO
 (2357)
 ROUS SARCOMA, GLYCOLIPID, TRANSFORMA-
 TION (2359)
 ROUS SARCOMA, IMMUNIZATION, CHICKEN
 (2436)
 ROUS SARCOMA, IMMUNOSUPPRESSION,
 HAMSTER (2360)
 ROUS SARCOMA, POLYOMA, KARYOTYPE,
 HAMSTER CELLS (2364)
 ROUS SARCOMA, POLYOMA, TRANSFORMATION &
 REVERSION (2155)
 ROUS SARCOMA, REPLICATION, NUCLEIC
 ACID INTERMEDIATES (2362)
 ROUS SARCOMA, RNA, CHICKEN, MOUSE
 (2365)
 ROUS SARCOMA, TRANSFORMATION,
 REVERSION, HAMSTER CELLS (2361)
 ROUS SARCOMA TYPE 0, DILUTION,
 PROGENY, QUAIL (2366)
 SARCOMA, LEUKEMIA, TRANSFORMATION,
 MOUSE, RAT (2350)
 SHOPE FIBROMA, COWPOX, CELLULAR DNA
 SYNTHESIS, INHIBITION (2380)
 SHOPE FIBROMA, CYTOCIDAL VIRUS, RABBIT
 (2379)
 SHOPE PAPILLOMA, ENZYME, RABBIT (2381)
 SIMIAN ADENOVIRUS, DNA, DENSITY (2296)
 SIMIAN ADENOVIRUS 7, HAMSTER CELLS
 (2324)
 SV40, ADENOVIRUS 2, HYBRID, VIRAL DNA
 (2332)
 SV40, CELL MEMBRANE, ANTIGEN, KIDNEY

(2447)
 SV40, DNA OLIGOMERS (2378)
 SV40, DNA QUANTITATION, TRANSFORMED
 CELL (2373)
 SV40, GROWTH, TRANSFORMATION, MOUSE
 CELLS (2370)
 SV40, IMMUNOSENSITIVITY, HAMSTER
 (2449)
 SV40, PLAQUE FORMATION, INHIBITION,
 REPRESSOR, REVIEW (2157)
 SV40, POLYPEPTIDE, PROTEIN (2369)
 SV40, RAUSCHER LEUKEMIA, TRANSFORMA-
 TION, RAT (2376)
 SV40, SUSCEPTIBILITY, CHROMOSOME
 TRISOMY (2375)
 SV40, TRANSFORMATION, RNA, DNA (2377)
 SV40 DEFECTIVE MALIGNANT TRANSFORMA-
 TION, HAMSTER CELLS (2372)
 VISNA, PROGRESSIVE PNEUMONIA, SLOW
 TRANSFORMATION (2297)
 VITAMIN B12
 3-METHYLCHOLANTHRENE, SKIN TUMOR,
 MOUSE (2234)
 WILM'S TUMOR
 NITRITE, 2-IMIDAZOLIDINE, RAT (2184)
 PLASMA RENIN, HUMAN (2556)







U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

OFFICIAL BUSINESS

PENALTY FOR PRIVATE USE, \$300

If you do not desire to continue receiving this publication, please CHECK HERE ☐;
tear off this label and return it to the above address. Your name will then be
promptly removed from the appropriate mailing list.

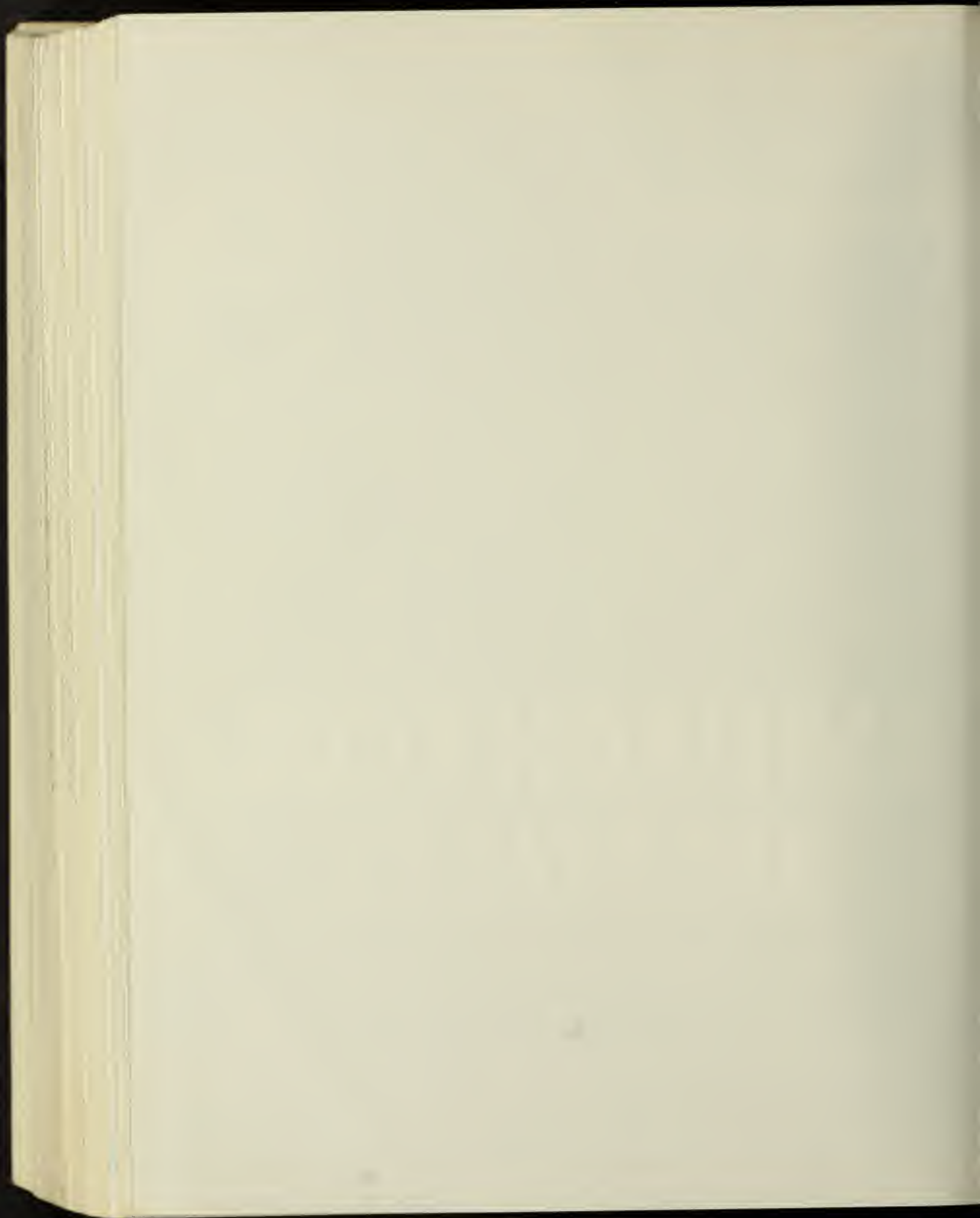
125
Veto
Med
SUBJECT AUTHOR INDEX

Vol. 9

CARCINOGENESIS ABSTRACTS

National Cancer Institute

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE • National Institutes of Health



AUTHOR INDEX

- RON, E.
 2133
 ROWSON, S.A.
 0199, 0557, 0589,
 0638, 0659, 0668,
 1037, 1095, 1528,
 2320, 2352, 2353
 RUKREA, C.
 1928
 RALLA, A.M.
 1505, 1508, 2374
 EL, C.A.
 2443
 RLEV, G.I.
 0596, 0598, 2003
 ELSON, H.T.
 0167, 0173, 1443
 RUKDEEN, E.R.
 1806
 RUKNIATHY, C.
 1647
 RASHI, D.V.
 1434, 2302
 RAHAM, S.
 2553
 RED, W.H.
 2122
 T, D.A.
 2128
 J-ZAIRA, H.T.
 0290
 RESON, E.D.
 0982
 RONG, B.G.
 0619, 1423
 RERMAN, A.B.
 0134
 RERMAN, L.V.
 0759, 2165*
 RERMANN, W.W.
 1451
 AM, E.
 0624
 AM, N.
 0719
 AMCOVA, B.
 1486
 AMOFF, N.
 2127
 AMS, M.L.
 1644
 AMSON, R.
 1602
 AMSON, R.H.
 0073, 1204
 CE, R.R.
 1843
 KUNLE, A.A.
 0425, 1779
 LBERG, M.
 2402
 NIS, L.
 0493, 0494
 DINGER, H.K.
 0157
 ER, W.H.
 2435
 ADNET, J.J.
 0127, 0128
 AEIKENS, B.
 1819
 AGARWAL, S.S.
 0703
 AGEENKO, A.I.
 0618, 2333
 AGEYENKO, A.I.
 1048, 1050
 AGEYEV, A.K.
 1271
 AGRANAT, V.Z.
 1634*
 AHEARN, M.J.
 1969
 AHMED, M.
 1965
 AHSTROEM, L.
 2015
 AHUJA, E.M.
 2480
 AISENBERG, A.C.
 0155, 0246
 AJELLO, L.
 1153
 AKAO, M.
 2207
 AKERVALL, K.
 1912
 ALBOT, G.
 1592, 1599*
 ALDRICH, C.D.
 2349
 ALEKSANDROV, S.N.
 1845, 1863*, 1864
 ALEKSANDROWICZ, J.
 1276
 ALEKSEEV, I.V.
 1290
 ALEXANDER, P.
 0725, 2406
 ALEXANDER, R.H.
 0326
 ALEXANDER-JACKSON, E.
 1946, 2119, 2120
 ALEXANIAN, R.
 1576
 ALEYASSINE, H.
 0043
 AL-FALLUJI, M.M.
 0682
 ALFIERI, A.
 1128
 ALFORD, C.A., JR.
 1460
 ALLEN, D.O.
 2498
 ALLEN, D.W.
 0582, 1027
 ALLEN, L.N.
 0338*
 ALLEN, P.
 2050, 2499
 ALLIETTA, M.
 0682
 ALLISON, A.C.
 1113, 1117
 ALM, G.V.
 1134
 ALONSO, A.
 1372*
 AL-SAAD, A.A.
 2557
 AL-SARRAF, M.
 2460
 ALTER, A.A.
 0150
 ALTER, M.
 2485
 ALTHOFF, J.
 1351, 1813, 2242,
 2245
 ALTMAN, N.H.
 0301*
 ALTWEIN, J.
 1613
 ALTWEIN, J.E.
 1186
 ALVARES, A.P.
 1805
 ALVAREZ, Y.
 0554, 1501
 AL-WAIDH, M.
 0771
 AMATRUDA, J.
 1653
 AMBRUS, J.L.
 0601, 0781, 2275
 AMBS, E.
 0270
 AMES, F.P.
 1925
 AMETANI, T.
 0249, 1018
 AMOS, E.B.
 1542
 ANASTASIO, CH.
 1844
 ANDELMAN, J.B.
 0865*
 ANDERER, F.A.
 1497, 1909
 ANDERS, P.
 2559
 ANDERSEN, H.A.
 1700
 ANDERSON, C.
 1176
 ANDERSON, C.K.
 1579
 ANDERSON, D.E.
 0780
 ANDERSON, J.
 0182, 0208, 1417
 ANDERSON, K.M.
 0932, 1990
 ANDERSON, N.G.
 0211
 ANDERSON, R.E.
 0267, 1001
 ANDERSSON, B.
 1007, 1544
 ANDRADE, Z.A.
 2122

ANDRE-SCHWARTZ, J.
 0224
 ANDREWS, P.
 0508
 ANDRIANOVA, M.M.
 1272, 1290
 ANGHILERI, L.J.
 1233, 2085
 ANGULO, M.
 0502
 ANKERST, J.
 0180
 ANONYMOUS
 0005, 0009, 0010,
 0015, 0108, 0113,
 0349, 0352, 0367,
 0372, 0375, 0376,
 0687*, 0688*, 0861,
 1130, 1142*, 1244
 ANSARI, H.
 0235
 ANTHONY, H.M.
 0980
 ANTHONY, P.P.
 0723
 ANTONELLO, C.
 0938
 ANTON-LAMPRECHT, U.
 2026
 AOKI, T.
 1034, 1427
 APFFEL, C.A.
 1758*
 APOSHIAN, H.V.
 0674, 0683
 ARAI, Y.
 0416
 ARAKI, K.
 2293
 ARAKI, M.
 0126, 1357, 1358
 ARCHAMBEAU, J.O.
 1384, 1385
 ARCHAMPONG, E.O.
 1416
 ARCHER, V.E.
 1859
 ARCHIBALD, F.M.
 2068
 ARCOS, J.C.
 0466, 0474, 1731,
 2192
 ARCOS, J.M.
 0956
 ARFFMAN, E.
 0036
 ARGUS, M.F.
 0466, 0474, 2152,
 2192
 ARIES, V.
 1189
 ARKHIPOV, G.N.
 0947
 ARLOTTA, P.
 1699
 ARMBRECHT, B.H.
 1778

ARMSTRONG, G.R.
 2302
 ARMSTRONG, J.A.
 1428, 2328
 ARMSTRONG, M.Y.K.
 0224
 ARNOLD, H.P.
 0427
 ARNOLD, W.J.
 0166
 ARON, M.
 0731*
 ARORA, G.D.
 1624
 AROUETE, J.
 1516*
 ARROYO, H.
 0343*
 ARTHUR, E.
 0565, 1701
 ASAHINA, M.
 1771
 ASHIKARI, R.
 1705
 ASSAL, N.R.
 0761
 ASVADI, S.
 2488
 ATANGANE, S.
 1266*
 ATASSI, S.A.
 0038
 ATHANASIU, P.
 2365
 ATKIN, N.B.
 0325, 2536
 ATKINSON, L.
 0321
 ATTARDI, G.
 2528
 ATTWOOD, M.M.
 2303
 AUBERT, C.
 0444, 1328
 AUBERT, L.
 0343*
 AUBERTIN, A.M.
 0522
 AUDET-LAPOINTE, P.
 0298*
 AUER, G.
 0813
 AUERBACH, O.
 0973, 0974, 1859
 AUERSPERG, N.
 0809
 AUGER, C.
 0992, 1631*
 AURELIAN, L.
 0186, 0623
 AURICH, G.
 0712
 AURORA, A.L.
 0274
 AUSTIN, B.J.
 0818
 AUSTIN, J.P.
 0292

AVILA, L.
 1882
 AWANO, I.
 1414
 AXELROD, D.
 1094
 AXELSSON, S.
 1222
 AYRES, J.L.
 1308
 AZAMA, Y.
 2253
 AZERAD, E.
 1279
 BAARS, A.
 1366
 BABA, K.
 1044
 BABAKOVA, S.B.
 0616
 BABCHIN, I.S.
 0644
 BABICK, L.A.
 2383
 BABKOVA, O.v.
 0654
 BACCHEITTI, S.
 2290
 BACHENHEIMER, S.L.
 2310
 BACIGALUPO, G.
 2223
 BACKMANN, B.
 1307
 BADER, A.V.
 0206, 0566
 BADER, J.P.
 0206, 0566,
 BAECHLER, C.A.
 1126
 BAESSLER, R.
 2470
 BAETENS, W.
 0544
 BAEZ, A.G.
 1199
 BAGSHAW, A.
 0231
 BAILAR, J.C., III
 1181
 BAILEY, J.M.
 1655
 BAKAY, M.
 0178, 1045
 BAKER, M.
 1903
 BAKER, M.C.
 0325
 BAKER, R.
 1903
 BALCHIN, L.A.
 2406
 BALDA, B.R.
 2540
 BALDAUF, W.
 1879
 BALDELLOU, A.
 1756*

BALDWIN, R.W.
 0361, 1132, 1550,
 2426
 BALFOUR, H.H., JR.
 1518*
 BALFOUR, I.C.
 0714
 BALKUS, M.
 0421
 BALL, J.K.
 1896, 2178, 2225,
 2266*
 BALL, R.A.
 0403
 BALLESTA, F.
 1756*
 BALLIS, M.E.
 2083
 BALLS, M.
 0565, 1701
 BALNER, H.
 0357
 BALTIMORE, D.
 1446
 BALUDA, M.A.
 1942
 BAMFORD, S.
 0245
 BANATVALA, J.E.
 0353
 BANERJEE, M.R.
 1802
 BANFIELD, W.G.
 1635
 BANKOWSKI, R.A.
 0159
 BANNASCH, P.
 1352, 1818, 2073
 BANNER, M.W.
 1005
 BANNIKOV, G.A.
 0833
 BARAHONA, H.H.
 1918, 1919
 BARAJAS, E.
 1193*, 1194*
 BARAK, Y.
 0779
 BARANSKA, W.
 0669, 1931
 BARATS, A.M.
 1265*
 BARBAN, S.
 1953
 BARBANTI-BRODANO, G.
 1092
 BARBATANO, L.
 1128
 BARBER, R.
 1605
 BARBIERI, D.
 1906
 BARCLAY, M.
 0785, 2068
 BARD, D.S.
 1125
 BARDOS, T.J.
 0781

BAREKAT, A.A.
 2041
 BARINSKIY, I.F.
 1418
 BARKER, B.E.
 1143
 BARKER, K.L.
 2551
 BARKER, L.F.
 0723
 BARKER, S.T.
 1431
 BARNARDT, J.H.
 0888
 BARNES, D.W.H.
 1381
 BARNES, J.E.
 1013
 BAROFESKY, I.
 1259
 BARON, S.
 0953
 BARRANCO, S.C.
 2250
 BARRILLIOT, L.
 1963*
 BARROU, B.A.
 1157
 BARROW, R.O.
 0573
 BARRY, D.H.
 0499
 BARRY, E.J.
 0407
 BARSKI, G.
 0858, 1715*, 1906,
 1908, 2416
 BARSTON, M.C.
 1474
 BARTLETT, G.
 0101
 BARTLEY, J.C.
 2553
 BASELGA, J.
 1757*
 BASERGA, R.
 0309
 BASHKAEV, I.S.
 0618, 1050
 BASILICO, C.
 1513, 2382, 2388
 BASKAR, J.F.
 1977
 BASOMBRIIO, M.A.
 0468
 BASSIN, R.H.
 0195, 1933, 2351
 BASSIR, O.
 0425, 1309, 1779
 BASTERIS, E.
 2004
 BASU, M.
 1958
 BATES, R.R.
 0891, 0931, 0934
 BAUCHINGER, M.
 0418

BAUER, H.
 1064, 1065
 BAUMAL, R.
 2421
 BAUMANN, R.
 0989*
 BAUSSERMAN, L.L.
 0891
 BAUTERS, F.
 1721*
 BAYRD, E.D.
 0507
 BEARD, D.
 0580, 0584, 1735,
 1890
 BEARD, J.W.
 0560, 0584, 1105,
 1735, 1890
 BEASLEY, J.D., III
 0737
 BEASLEY, J.N.
 1915
 BEATTIE, E.J., JR.
 0286
 BEATY, A.
 2186
 BEAUDREAU, G.S.
 0586, 1892, 1893,
 2082
 BECHT, H.
 1497
 BECK, E.G.
 0936
 BECK, J.S.
 0774
 BECKENBACH, H.
 0366
 BECKER, F.F.
 1299, 1303
 BECKER, H.
 0772
 BECKWITH, J.B.
 0326
 BELADI, I.
 0178, 1045
 BELDOTTI, L.
 0224
 BELEHRADEK, J., JR.
 1906, 2416
 BELICZA, M.
 1671
 BELL, J.A.
 1673
 BELL, R.B.
 0316
 BELOHORSKY, B.
 0810
 BENATRE, A.
 2111
 BENDA, P.
 1991
 BENDER, E.
 0672
 BENDICH, A.
 0721, 1202, 2224
 BENEDICT, W.F.
 2098

568

* indicates a plain citation without accompanying ab

ANEY, B.
 1012
 CH, K.J.
 1097
 DI, F.C.
 0274
 EMENDAL, H.
 0607
 MGREN, H.
 1544, 1573
 OM, B.
 2421
 OM, E.T.
 0072, 1986
 EFARB, S.M.
 1723
 UM, E.
 0421
 ME, A.
 0783
 UNCK, J.M.
 0053, 1316
 EDER, E.
 1956
 BROV, YU.F.
 2469
 CHAROV, A.F.
 1418
 CK, F.G.
 1793
 CKMUHL, F.
 0285
 ENBERGER, A.
 0412
 ECKER, B.B.
 1013, 1014, 1015
 CHM, N.
 1640
 ESENBERG, H.
 0881*
 EITGER, D.
 0641, 0647
 GART, B.
 1321
 GDN, A.E.
 0630
 GER, E.
 1795
 GGS, D.R.
 0328
 GOVSKY, P.A.
 0384*
 HLG, H.
 2481
 HUON, C.
 0444, 1328
 IRON, M.
 0758, 1068, 1476
 LDEN, A.
 2561
 LIS, G.B.
 0192, 0628, 0632,
 2286
 LLER, K.
 0903
 LOGNESI, D.P.
 1064, 1065, 1485,
 1887, 2312

BOLONINA, N.I.
 0436
 BONAR, R.A.
 1105
 BONHAG, R.S.
 1530
 BONK, U.
 0253
 BONMASSAR, A.
 2448
 BONMASSAR, E.
 2448
 BONNEAU, H.
 0241*, 2364
 BONNET-GAJDOS, M.
 0870*
 BOOK, J.A.
 0521
 BOONE, C.W.
 1500
 BOOTH, C.C.
 0740
 BOOTHE, A.D.
 0563, 1875
 BOQUIST, L.
 1246
 BOREK, E.
 0319, 2511
 BOREK, Z.
 0768*
 BORENFREUND, E.
 1202
 BORGESKOV, S.
 0773
 BORNSTEIN, F.P.
 1171
 BOROVIKOVA, N.M.
 2294*
 BORSOS, T.
 1555
 BORUM, K.
 2455
 BOSIN, T.R.
 0863*
 BOSMANN, H.B.
 1114, 1641
 BOTSCHAN, N.E.
 0897
 BOTTGER, M.
 1426
 BOTTIGER, M.
 1495
 BOUCHAYER, M.
 1154
 BOUCOT, K.R.
 0764
 BOULESTEIX, J.
 0870*
 BOURGEOIS, C.H.
 1777
 BOURRET, J.
 1370
 BOURSE, R.
 1375*
 BOUSQUET, W.F.
 0071
 BOWDEN, D.H.
 0542

BOWEN, J.W.
 2400*
 BOWEY, C.E.
 2467
 BOY, M.J.
 2214
 BOYSE, E.A.
 1427
 BRACHMANN, I.
 0031
 BRADBURY, S.
 2109
 BRADY, R.O.
 0568, 1091
 BRAENDSTRUP, O.
 2102
 BRAMBILLA, G.
 0401
 BRANDT, L.
 1240
 BRANTON, P.E.
 1106, 1110
 BRAUN, W.
 0356, 2403
 BRAUNSTEINER, H.
 2584*
 BRAWERMAN, G.
 2071
 BRAWN, R.J.
 0471
 BRAYLAN, R.C.
 1442
 BREGA, A.
 2570
 BREGULA, U.
 2514, 2554
 BREHM, G.
 0334*
 BREIDENBACH, G.P.
 2340
 BREIER, B.
 0217
 BREMNER, C.G.
 0759
 BRENNAN, J.T.
 0524
 BRENNAN, M.J.
 1419
 BRENNEIS, H.J.
 1385
 BRESNICK, E.
 0463, 1337, 1341,
 2547
 BREWEN, J.G.
 2203
 BREZAK, M.A.
 1199
 BRIAND, P.
 0854
 BRIGGS, G.M.
 2191
 BRILES, W.E.
 0160
 BRINKLEY, B.R.
 0786
 BROADATY, E.
 2328

BROCKMAN, W.W.
1444
BRODEY, R.S.
1975, 2044
BRODY, I.
0735
BRODY, J.I.
0775, 1116, 1212
BROMFELD, E.
1446
BROOKES, P.
0941, 2149
BROOKS, A.L.
1394
BROOKS, S.E.H.
0719
BROSS, I.D.J.
1604
BROUWER, E.J.
0419
BROWER, L.P.
0512*
BROWN, B.L.
1548
BROWN, C.D.
2098
BROWN, D.G.
0994
BROWN, D.Q.
2229
BROWN, D.W.
2063
BROWN, E.
0364, 0365, 0861
BROWN, E.V.
0029, 0924
BROWN, J.M.
0068
BROWN, N.R.
0206
BROWN, S.M.
0391*
BRUCHER, J.M.
2080, 2247
BRUCKNER, L.
0768*
BRUGERE, J.
1628*
BRUNI, J.E.
2501
BRUNSCHWIG, J.P.
1885
BRYAN, G.T.
0037, 0038, 0417,
0423, 0899
BRYAN, W.R.
2366
BRYANT, G.M.
2192
BRYANT, J.I.
1201
BUCCIARELLI, E.
0632
BUCHALT, L.
2573*
BUCK, C.A.
1939, 1957

BUCK, R.C.
1209
BUCKLEY, C.E., III
1123
BUDER, E.
1851
BUCHLER, J.
1823
BUCHNER, M.
2153
BUJELL, D.N.
1435
BUERKLE, G.
1819, 2184
BUESCHER, H.
1692
BUESSE, E.
2143*
BUETTERICH, D.
2584*
BUFFE, D.
1577
BUJADOUX, M.
1547
BUKIN, YU.V.
2317
BULAY, O.M.
1332, 1797
BULHELLER, H.
1879
BULLIS, C.
0310
BUNNEY, W.E.
1835
BURDON, R.H.
2097, 2100
BURG, C.
1547, 1987, 2432
BURG, H.E.
0907
BURGER, C.L.
0164, 1474, 1894
BURGER, D.R.
1324
BURGER, M.
1657
BURGER, M.M.
0679, 0680
BURGHOUTS, J.T.M.
0607
BURGOYNE, G.H.
0161
BURKITT, D.P.
0006, 1608, 2040
BURLINGHAM, B.T.
2325
BURMEISTER, R.E.
0744
BURMESTER, B.R.
1465, 1467, 2310
BURN, C.
1607
BURNET, F.M.
0355
BURNETT, J.B.
2541
BURNS, E.R.
1663, 2555

BURNY, A.
0141, 0142,
BURRI, P.H.
2587*
BURROWS, J.H.
1419
BURRY, A.F.
0795
BURSTEIN, N.A.
0635
BURSTIN, S.J.
2382
BURTIN, P.
0240*, 1577
BURTON, A.C.
1728
BUSBY, W.F., JR.
1205
BUSCHER, T.J.
1454
BUSHONG, S.C.
2449
BUSS, H.
0272
BUSSE, V.
1766
BUSSMANN, J.F.
2029
BUSTAD, L.K.
1274
BUTEL, J.S.
0615, 1100,
1525, 2372
BUTLER, T.P.
2226
BUTLER, W.H.
0950, 0952,
1808, 1809,
2240
BUU-HOI, N.P.
0411, 2269*
BUXTON, D.F.
1663
BYKOVSKY, A.P.
0144
BYVOET, P.
2056
CACCIATORE, R.
2125
CAEN, J.
1643
CAFFIER, H.
1911
CAICUTS, R.
2505
CAJAL, H.
1490, 1498
CALAFAT, J.
0627, 2246
CALAMARI, F.
1184
CALDWELL, B.V.
1993
CALMAN, F.
2142*
CALNEK, B..
0157, 0158

ACHO, E.
 2123
 AIN, R.
 2004
 BELOVA, J.
 2417
 E, P.E.
 2346
 ERON, D.A.
 0548
 ERON, E.H.D.
 0782
 PADELLI-FIUME, G.
 0961
 PAIGNE, E.
 0863*
 PBELL, J.A.
 0620, 2387
 PBELL, J.G.
 1031
 PBELL, J.L.
 0825*
 AANI, E.
 0651
 TY, T.G.
 1531, 1559
 PELACRE, P.
 1742
 PUTO, A.
 0219, 2200
 RACENI, C.E.
 0401
 RBON, J.
 2148
 RBONE, G.
 1584
 RBONE, P.
 2535
 RBONE, P.P.
 0154, 1434
 RDEILHAC, P.T.
 0048
 RDELLA, T.
 0045
 RDIFF, R.D.
 1144
 RDINI, G.
 1713*, 2577*
 RLASSARE, F.
 0938
 RLSSON, C.A.
 1567
 RO, W.
 1162
 RO, W.A.
 1723
 ROLI, J.
 1598*, 1780
 RR, T.E.F.
 1381
 RROLL, K.K.
 0062, 2134
 RROZZA, G.
 2033*
 RRUTHERS, C.
 0726
 ARSON, T.R.
 0424

CARTER, A.P.
 1632*
 CARTER, R.L.
 0488, 0610, 1680
 CARTER, W.A.
 1444
 CASALS, J.
 1995
 CASE, M.T.
 1151
 CASPARY, E.A.
 1197
 CASPERSSON, T.
 0262*
 CASSINGENA, R.
 2157
 CASTELLI, L.
 0219
 CATALANO, L.W.
 1061
 CATER, D.B.
 2476
 CATOVSKY, D.
 1365
 CATTOOR, J.P.
 0187
 CAULET, T.
 0127, 0128, 0486
 CAVANNA, M.
 0401
 CEDERLOF, R.
 0109, 0500
 CEGLOWSKI, W.S.
 1022, 1529, 1534,
 1535
 CEGRELL, L.
 1222
 CEMAN, C.
 0223
 CENTENO, J.V.
 1689
 CERNY, E.
 0922
 CERVANTES, Q.F.B.C.
 0125
 CESARINI, J.P.
 1421, 2560
 CESARO, A.N.
 0878*
 CHABOT, J.F.
 0580
 CHAMBERLAIN, C.C.
 1474
 CHAMLIAN, D.L.
 0743
 CHAN, E.W.
 2178, 2266*
 CHAN, G.Y.
 1111
 CHAN, J.C.
 1107, 1111
 CHAN, P.C.
 0935
 CHANDAVIMOL, P.
 1777
 CHANDRA, P.
 1551

CHANDR, S.
 0175, 1925
 CHANDRASEKHARA, N.
 1305
 CHANLEY, S.G.
 1210
 CHANG, J.P.
 0429
 CHANG, L.O.
 1652
 CHANG, N.H.
 0551, 2458
 CHANG, R.S.
 1073
 CHANG, S.S.
 1070, 1543
 CHANY, C.
 0612
 CHANY, E.
 2072
 CHAPMAN, E.M.
 0549
 CHARDONNET, Y.
 1963*
 CHARDOT, C.
 1159
 CHARNEY, J.
 0194, 1067, 1419,
 1929
 CHARUZY, I.
 0449
 CHAUVEAU, J.
 0921
 CHAUVERGNE, J.
 0019*
 CHAUDRY, I.
 1338
 CHECHELASHVILI, G.L.
 2196
 CHEEVERS, W.P.
 0218, 1106, 1110
 CHEN, J.K.M.
 2268*
 CHEN, K.
 2425
 CHEN, K.K.
 1293
 CHEN, K.P.
 2491
 CHEN, L.
 0928
 CHEN, M.M.-S.
 1234
 CHEPINOGA, O.P.
 0972
 CHERKASSKIY, L.A.
 1586
 CHERNOZEMSKI, I.N.
 0081, 0399, 0971
 CHERNTSOVA, T.A.
 2574*
 CHERRY, C.P.
 0441, 0887, 1790
 CHERVENICK, P.A.
 0328
 CHESTERMAN, F.C.
 0610

CHEUNG, A.S.M.
1234
CHEVREL, B.
1598*
CHEW, B.K.
0232
CHEW, E.C.
1665
CHIARUGI, V.P.
2025, 2529
CHIECO-BIANCHI, L.
1970
CHIFFELLE, T.L.
1014, 1015
CHIHARA, G.
0026, 1583*
CHIKKAPPA, G.
0290
CHIN, C.T.
0978, 0979
CHIRIGOS, M.A.
1171, 0196, 0602,
1036, 1069, 1933
CHIVOT, J.J.
1643
CHO, H.Y.
1326
CHOE, B.K.
2526
CHOI, Y.S.
1667
CHOLON, J.J.
1869
CHOPDAR, A.
0749*
CHOPRA, H.C.
0146, 0626, 0630,
1420, 1427, 1443,
1870
CHORDI, A.
0707
CHOUROULINKOV, I.
0460, 0926
CHRIST, M.L.
1239
CHRISTINE, B.W.
1611
CHRISTOFFERSEN, P.
2102
CHRISTOPHERSON, W.M.
0297*, 2480
CHU, C.T.
1972
CHU, E.H.Y.
1393
CHU, F.C.H.
0133
CHUAT, J.C.
0758, 1476
CHUNG, C.W.
0424
CHUNG, E.B.
0273
CHYLE, M.
1836*, 1837*
CHYLE, P.
1836*, 1837*

CIEGLER, A.
0388*, 2267*
CIKES, M.
1077, 1445
CILIEVICI, O.
1844
CIOBANU, Z.
1979
CIOLOCA, L.
2236
CIOVIRNACHE, M.
1297
CISCARIUS, F.
0748*
CISIANO, L.
0342*
CITOLER, P.
0137, 1822
CLAFLIN, A.J.
2510
CLAPP, N.K.
0080, 1348
CLARK, C.G.
1416
CLARK, E.
2522
CLARK, H.F.
0937, 1425
CLARK, V.A.
0281
CLARK, W.E., II
2566
CLARK, W.F.
1961
CLARKE, D.H.
1995
CLARKE, G.D.
0216
CLARKSON, B.D.
1996
CLASON, A.E.
1440
CLAYSON, D.B.
0380*
CLEAVER, J.E.
1388
CLEMMESSEN, J.
0868*, 1267
CLIFFORD, P.
0574, 0578, 1423,
1697, 1973, 2305
CLIFFORD, W.
1024
CLIN, B.
0520*
CLINE, M.J.
2461
CLYMER, R.
2412, 2456
COADY, A.
0033
COBB, L.M.
0543
COCHET, G.
0241*
COCHRAN, A.J.
2314

COEZY, E.
0378*
COFFELT, C.F.
0281
COFFEY, C.B.
0050, 1317
COFFIN, D.L.
2230
COFFIN, J.M.
2358
COGGIN, J.H.
0211
COHEN, D.
1163
COHEN, G.H.
2337
COHEN, J.J.
1616
COHEN, M.H.
0154
COHEN, M.M.
0694
COHEN, S.
1126, 2451
COHEN, S.M.
0037, 0038, 0039
COHN, M.
1568
COLE, P.
0976, 1187, 1188
COLE, S.R.
0260
COLEY, G.M.
2566
COLLAVO, D.
1970
COLLINS, J.J.
1097
COLMEAUER, M.E.M.
1442, 1557
COLNAGHI, M.I.
0099
COMBS, G.E.
0048
COMMONER, B.
0042
CONARD, R.A.
0529
CONE, C.D., JR.
1269
CONE, C.E., JR.
1677
CONLEY, J.
0547
CONNELL, D.I.
1322
CONNELLY, R.R.
1612
CONNEY, A.H.
0939, 1334, 1335
1796
CONRAD, P.A.
1961
CONSIGLI, R.A.
1112, 1511
CONVENTI, L.
1517*

CONVERSE, C.F.
 1249
 CONZELMAN, G.M.
 0027
 COOK, P.J.
 1608
 COOKE, K.O.
 1880
 COMBS, M.M.
 1763
 COONEY, D.A.
 2186
 COOPER, D.A.
 0764
 COOPER, E.H.
 0380*, 1230, 1300,
 1579
 COOPER, R.W.
 0073
 COOPERBAND, S.R.
 1574
 CORBETT, T.H.
 0400
 CORNEFERT-JENSEN, F.
 1876
 CORNICK, G.
 1913
 CORRIN, B.
 2103
 CORY, J.G.
 1907, 2321
 COTALLASSO, D.
 0122*
 COUER, P.
 1374*
 COULET, M.
 0242*
 COUTELLE, C.
 0253
 COUTELLE, R.
 0253
 COWAN, D.M.
 0442
 COWAN, L.B.
 1614
 COWDELL, R.H.
 2109, 2467
 COWEN, D.M.
 1300
 COYOTE, N.
 0406
 CRADDOCK, V.M.
 0831
 CRAFT, J.L.
 1461
 CRAIG, A.M.
 0410
 CRAIG, A.W.
 0481, 0605, 0949
 CRAIG, N.C.
 1659
 CRANE, P.S.
 1174
 CRARY, D.D.
 0802
 CRATHORN, A.R.
 2248, 2254

CRAWFORD, J.D.
 0549
 CRAWFORD, M.
 0273
 CREECH, C.
 1435
 CREMER, N.E.
 1447
 CREPIN, G.
 0747*
 CRITTENDEN, L.B.
 0160
 CROISIER, J.C.
 1279
 CROISY, A.
 2269*
 CROIZAT, H.
 1011
 CROQUETTE, M.F.
 1721*
 CROSSEN, P.E.
 1206
 CROSSWHITE, L.H.
 1235
 CROWTHER, J.S.
 1189
 CRUMPACKER, C.S.
 1052, 2332, 2371
 CUMAR, F.A.
 0568
 CUMMING, R.B.
 0902
 CUNNINGHAM, C.H.
 1467
 CUNNINGHAM, D.D.
 1960
 CUNNINGHAM, M.P.
 1140
 CUTRIGHT, D.E.
 0737
 CWCYNARSKI, M.T.
 2451
 CZACHOR, M.
 1276
 CZOPIK, J.
 1600*
 DAAMS, J.H.
 0627, 0629, 2453
 DABBERT, A.F.
 2481
 DABHOLKAR, R.D.
 2036
 DABICH, L.
 0310
 DABSKA, M.
 2575*
 DAFTARY, D.K.
 0247
 DAGNA-BRICARELLI, F.
 0699
 DALEZIOS, J.
 1310
 DALHAMN, T.
 0107
 DALLAPICCOLA, B.
 1719*
 DALLENBACH-HELLWEG, G.
 1160, 2027

DALQUEN, P.
 2481
 DALTON, A.J.
 2302
 DAMERAU, W.
 2187
 DAMJANOV, I.
 0317, 1671, 2478*
 DANIEL, M.D.
 1057, 1059, 1464,
 1917, 1919
 DANIEL, M.R.
 2075
 DANNENBERG, H.
 0412
 DAO, T.L.
 1791
 DARJALOVA, S.L.
 1634*
 DAS, K.C.
 0698, 0701
 DAS, M.R.
 0141, 0142, 0553
 DATTA, S.K.
 0685, 2454
 DAUMAS, B.
 0343*
 DAUNE, M.
 1772
 DAVEY, D.A.
 0527
 DAVEY, F.R.
 0323
 DAVID, C.
 2111
 DAVID, C.S.
 2439
 DAVIDSON, C.
 0442
 DAVIDSON, H.
 1315
 DAVIES, D.A.L.
 1141*
 DAVIES, J.N.P.
 1607, 2019
 DAVIES, R.E.
 1860
 DAVIES, R.F.
 1806
 DAVIS, D.
 2336
 DAVIS, H.J.
 0186
 DAVIS, J.M.G.
 1852
 DAVIS, J.W.
 0154
 DAVIS, P.A.
 0288
 DAVIS, R.D.
 2186
 DAVIS, R.L.
 2124
 DAWBER, R.P.R.
 0777
 DAWE, C.J.
 1273, 1512

DAYAL, Y.
 0426
 DAYTON, S.
 1363
 DE ASUA, F.J.
 1928
 DE BALANZO, J.
 0734*
 DE BARBIERI, A.
 1506
 DE BAULT, L.E.
 2495
 DE CARNERI, I.
 1238
 DE CHOLNOKY, T.
 0986*
 DECKER, C.
 0522
 DECKERS, P.J.
 0728, 2428, 2459,
 2464*
 DECLOITRE, F.
 0923
 DE COSSE, J.J.
 0691, 1249
 CEDUKH, N.V.
 0817
 DEENEY, A.O.
 2082
 DE ESTABLE-PUIG, J.F.
 0992
 DE ESTABLE-PUIG, R.F.
 0992
 DEFENDI, V.
 0670, 1089, 1954
 DE FLORIO, B.
 1635
 DEFOORT, J.
 2127
 DE GEORGE, F.V.
 0801
 DEGTYARENKO, V.I.
 1526
 DE HALLEUX, F.
 2360
 DE HARVEN, E.
 1898, 1975, 2348
 DEHNEN, W.
 0069, 0936
 DEICHMANN, W.B.
 0421
 DEKNUDT, G.
 1392
 DE KOCK, D.H.
 0888
 DELAIN, E.
 0587, 1436
 DELALIEUX, G.
 1223
 DELAMORE, I.W.
 0717
 DELESCLOSE, C.
 1516*
 DELFS, E.
 1653
 DEL GIACCO, G.S.
 0733*

DELLA PORTA, G.
 0099
 DELLA ROSA, R.J.
 1274
 DELL'ORCO, R.T.
 2509
 DELMAS-MARSALET, Y.
 1721*
 DE MADRID, A.T.
 1428
 DE MAEYER-GUIGNARD, J.
 0021*
 DEMAILLE, A.
 0494, 0495, 0747*
 DEMENT'YEV, I.V.
 1418
 DEMINATTI, M.
 1721*
 DEN, H.
 1958
 DENEKAMP, J.
 1409*
 DEN ENGELSE, L.
 2246
 DENISON, E.K.
 1712*
 DENMAN, A.M.
 0168
 DENMAN, E.J.
 0168
 DE NORONHA, F.
 0711, 2312
 DENT, P.B.
 1997
 DEO, M.G.
 0426
 DE OCA, H.M.
 0063
 DE OME, K.B.
 0076, 0769, 2191
 DE PAPP, Z.G.
 0138*
 DEPLANO, A.
 0766*
 DERINGER, M.K.
 0193, 1198
 DE RUDDER, J.
 1759*
 DESAI, L.S.
 2515, 2530
 DESAI, S.M.
 0652
 DE SCHRYVER, A.
 0579
 DESGRANGES, C.
 0625
 DESHPANDE, V.A.
 2042
 DE SOMER, P.
 0685
 DE THE, G.
 0579, 0625, 1481,
 1922
 DE TKACZEWSKI, L.Z.
 1442
 DETOLLE, P.
 0343*

DETROY, R.W.
 0388*, 2267*
 DEUTSCH, A.
 2517
 DEUTSCHER, S.
 1625
 DE VILLIERS, J.N.
 0248
 DEWYS, W.
 1232
 DEY, A.K.
 1292
 DIAMANDPOULOUS, G.
 0209
 DIAMOND, L.
 0346, 0445, 09
 DIANZANI, M.U.
 1725
 DIEHL, V.
 2015
 DIETZ, M.
 2313
 DIETZ, W.
 0965
 DILLARD, R.D.
 1287
 DILLER, I.C.
 2121
 DILLEY, W.G.
 1676
 DIL'MAN, V.M.
 2469
 DI MARCO, A.T.
 1989
 DINOWITZ, M.
 0650
 DI PAOLO, J.A.
 1322, 1331, 21
 DIPPLE, A.
 0933
 DI RE, F.
 1238
 DITTRICH, W.
 1722*
 DJORDJEVIC, J.
 1850
 DMITRIEV, V.N.
 1145
 DMOCHOWSKI, L.
 0561, 1866, 19
 1976, 2295, 24
 2410
 DOBOS, M.
 0330
 DOBROTA, M.
 1636
 DOBROVOLSKAIA, N.
 2127
 DOBYNS, B.M.
 0529
 DOCHERTY, J.J.
 1463
 DODD, D.C.
 2012
 DODD, M.C.
 0682

DODGE, O.G.
 1607
 DODGE, W.H.
 0643
 DOELL, R.G.
 0590
 DOERFLER, W.
 1051, 2325
 DOI, T.
 1028, 1030, 1063
 DOIDA, Y.
 2283
 DOKLEN, A.
 0700
 DOKOV, V.K.
 0469
 DOLIN, R.
 1056
 DOLL, R.
 2043
 DOMBROWSKI, C.S.
 0124
 DOMINGO ALBOS, A.
 0748*
 DOMINGO GOMEZ, J.
 0748*
 DOMSCHKE, W.
 0475
 DONALDSON, W.E.
 0916
 DONATI, E.
 0299*, 1401*
 DONAWICK, W.J.
 2012
 DONCHEVA-STRATEVA, N.
 2483
 DONNER, L.
 0201
 DONNER, M.
 2432
 DONNELLY, A.J.
 2121
 DONNER, L.
 1921
 DONNER, M.
 1987
 DONOVAN, P.J.
 1331, 2197
 DONTENWILL, W.
 1366
 DORDAL, E.
 1708*
 DORKEN, H.
 0272
 DORN, C.R.
 2039, 2288
 DOSIK, H.
 0150
 DOSNE PASQUALINI, C.
 1442, 1557, 2136
 DOSTALOVA, O.
 0229
 DOUGHERTY, C.M.
 0504
 DOUGHERTY, E., III
 0588
 DOUGHERTY, R.M.
 1964

DOUGHERTY, T.F.
 1003
 DOUGHTY, W.E.
 1001
 DOUGLAS, J.R.S.
 1681
 DOORMASHKIN, R.R.
 2007, 2008
 DOVE, W.F.
 0400
 DOWDLE, W.
 0002
 DOWDLE, W.R.
 1054
 DOWLING, M.
 0665
 DOWNIE, J.C.
 2303
 DOWNS, W.G.
 1995
 DOYENNETTE, M.C.
 0495
 DOYEN, G.
 2080
 DRAKE, B.J.
 1723
 DRAPER, G.J.
 1180
 DRASAR, B.S.
 1189
 DRECHSLER, H.J.
 1822
 DREWINKO, B.
 1257
 DREWS, J.
 0696, 2205
 DRIESSENS, J.
 0493, 0495
 DRINGS, P.
 0696
 DRUCKREY, H.
 0032, 0090, 0483,
 0905, 2252, 2265*
 DUBBS, D.R.
 0664, 0666
 DUBERT, J.M.
 0819
 DUESBERG, P.H.
 0202, 0651, 1066
 DUFF, R.
 0213, 0615
 DUKSIN, D.
 0661
 DULBECCO, R.
 0673, 0678, 1109
 DULLY, M.
 1247
 DUNBAR, F.P.
 2125
 DUNBAR, L.M.
 1655
 DUNCAN, M.E.
 0941
 DUNKEL, V.C.
 1882
 DUNN, C.D.R.
 0413

DUPLAN, J.F.
 0592, 0819, 0999
 DUPLANTIER, D.P.
 0896
 DUPONT, B.
 0773
 DURBIN, C.G.
 1778
 DURR, F.E.
 0621, 1023
 DUSHKIN, V.A.
 2166*
 DUTCHER, R.M.
 1870, 1873
 DUTTA, S.K.
 1877
 DUTZ, W.
 2041
 DUVEL, D.
 0397
 DUX, A.
 2112
 DVORAK, R.
 2408, 2433
 DYADKOVA, A.M.
 1947
 DZAGNIDZE, L.N.
 2196
 DZHIBILOV, I.I.
 2166*
 DZHIOEV, F.K.
 1320
 EASON, R.
 1492, 1494
 EAST, J.
 0393*
 EATON, S. DEL A.
 0931
 EBBESEN, P.
 0593
 EBERT, J.D.
 2164*
 EBERT, P.S.
 1933
 ECKER, S.
 0745
 ECKHARDT, W.
 1109
 ECKHART, W.
 2384
 ECKNER, R.
 1900
 ECSENYI, M.
 2571
 EDDS, G.T.
 0048
 EDGE, J.R.
 1263*
 EDGERTON, B.W.
 2459
 EDGINGTON, D.N.
 1006
 EDWARDS, F.
 1888
 EDWARDS, J.G.
 2387
 EHRLING, F.
 1722*

EILBER, F.R.
0147, 0704, 0,10,
1880, 1984
EINHORN, N.
0578
EISEN, H.N.
2006
EISENBERG, H.
1612
EISENBRAND, J.
0989*
EL ATTAR, O.A.
0268
ELEJALDE, R.
1256
EL-FIKY, S.M.
0190, 1469, 1470
ELGJO, K.
1208, 1216, 2059
ELGORT, D.A.
0596
ELKIND, M.M.
0524
ELLIOTT, S.C.
1451
ELLIS, F.H., JR.
1700
ELLIS, L.D.
2110
ELLSWORTH, H.S.
0503
EL'PERIN, B.M.
0763
ELSASSER, P.
1570
ELSON, L.A.
0413
ELWOOD, J.C.
1651
ELY, T.S.
0115
EMAFO, P.O.
1309
EMARA, A.
1277
EMBLETON, M.J.
1132, 1550, 2426
EMERY, E.W.
1409*
EMMELDT, P.
2246
ENCHEV, S.
0820
ENDERS, J.F.
0209
ENDO, H.
1746
ENGELHARDT, N.V.
2003, 2004
ENNEKING, W.F.
1707*
ENOMOTO, M.
1359, 1827
EPLING, G.P.
0525
EPSTEIN, E.
0519*

EPSTEIN, M.A.
0619, 1423
EPSTEIN, S.M.
1296
EPSTEIN, S.S.
0518*
ERASMUS, D.
1253
ERB, R.J.
0075
ERIKSON, E.
0585
ERIKSON, R.L.
0585
ERNBERG, I.
1971
ERTURK, E.
0037, 0038, 0417,
0423
ESBER, H.
1993
ESCHENBACH, C.
1041
ESCOUROLLE, R.
1402*
ESHBACH, T.B.
1504
ESTES, M.K.
1502, 2369
EULITZ, H.
2020*
EULITZ, M.
2020*
EVANS, A.E.
0283
EVANS, A.S.
0546
EVANS, D.L.
1915
EVANS, E.P.
1381
EVANS, R.
0725
EVANS, V.J.
0063, 1200
EVATT, B.L.
0266
EVERETT, M.A.
1855
EWALD, J.L.
0703
EZDINLI, E.Z.
1235
FABIANI, A.
0089, 0963, 0964
FABRIKANT, J.I.
2051
FABRIZIO, D.P.A.
1925
FAHMY, M.J.
0439
FAHMY, O.G.
0439
FAHR, K.
0988*
FAIRCHILD, R.G.
1385

FAIRLEY, G.H.
1129, 2406
FAKHRI, O.
0291, 0729*
FALKE, D.
0188
FALZI, G.
1404*
FAN, K.
1124
FANSHIER, L.
0645, 0646, 06
1081, 1088, 14
1941, 1943, 23
FARAGO, L.
0117*
FARAS, A.
1943, 2357
FARBER, E.
1296
FARBER, J.
0783
FARRELL, R.L.
0608
FARROW, J.H.
1705
FASSKE, E.
0220, 0829*
FAUMENI, J.S., JR.
1181
FAUSTO, N.
0039
FAVRE, M.C.
0625
FAVRE, R.
0241*
FAYS, J.
1601*
FECHNER, R.E.
0984
FEDOROVA, A.V.
2294*
FEDEKOVSKAYA, M.I.
0943
FEHER, J.
2180, 2182
FELDMAN, D.G.
0550, 1039
FELDMAN, R.
1330
FELDMANN, F.M.
2124
FELICETTI, D.
0253
FELMEISTER, A.
1338
FENNER, F.
0864*
FENYO, E.M.
1445
FENYVES, A.
1979
FERBER, E.
2057
FERGUSON, D.B.
1868
FERGUSON, S.W.
0796

RAGUT, A.
0734*
RARA, A.
1690
RERO, A.
0086
RIERE, G.
1402*
SHTUDT, V.I.
2482
TING, R.
0220
F.
0672
LKOW, P.J.
1201, 1687, 2305
HIDZHYAN, B.S.
0453
LER, I.J.
0822
L, R.J.
0601, 1032, 1430
LD, E.J.
1197
LD, S.B.
1409*
SSINGER, J.N.
2445
LATOV, F.P.
1418
BERT, J.E.
2298
CH, Y.H.
2428
IPE, M.I.
2069
LITTI-WURMSER, S.
2445
MIANI, V.
0215
NGERHUT, B.
2572
NK, L.M.
2199
NK, M.A.
0163, 2409
NKEL, G.C.
1776
NKELSTEIN, M.
2263
NLAYSON, A.
1170
NLEY, A.G.
1206
NOGENOVA, M.A.
2233
SCHER, H.
0662, 2057
SCHER, P.
1261, 2243
SCHINGER, P.J.
0195, 1934
SHER, B.
2462
SHER, E.R.
2462
SHER, M.YE.
0763

FISHMAN, W.
2567
FIUME, L.
0961
FLANDERS, L.E., III
0027
FLEMING, J.
0321
FLETCHER, C.M.
0017
FLETCHER, D.E.
1263*
FLETCHER, O.J.
2439
FLICKINGER, J.T.
1899
FLIESSBACH, R.
0272
FLINT, G.L.
2261
FLODERUS, B.
0500
FLOHE, L.
1819
FLOREY, M.
1903
FLOYD, R.
1532, 1923
FLOYD, W.S.
1619
FOELSCH, E.
0696
FOERSTER, C.
1041
FOFT, J.W.
0396
FOGH, H.
0665
FOGH, J.
0665
FOITZIK, E.
0564
FOLANOVA, K.A.
0534
FOLEY, G.E.
2494, 2515, 2530
FOLKMAN, J.
1647
FONCK-CUSSAC, Y.
0242*
FONG, C.K.Y.
0210, 1099, 2335
FONTAINE, J.L.
0870*
FOOTE, F.W., JR.
0746
FORBES, J.F.
0718
FOREMAN, C.
2457
FORNI, A.
2193
FORSYTH, B.
0045
FORT, L.
2247
FOSSATI-GUGLIELMONI, A.
0699

FOSTER, R.S., JR.
0332
FOURCADE, A.
0587
FOURNIER, E.
1834
FOUTS, J.R.
0848
FOX, B.W.
2291
FOX, R.R.
0802
FOX, T.O.
1952
FOWLER, M.E.
0033
FRABLE, W.J.
0693, 2105
FRADKYN, S.Z.
0763
FRALEY, E.E.
0745
FRANCESCHI, C.
1989
FRANK, H.
1909
FRANKC, R.
0348, 2153
FRANKEL, H.H.
0041, 0409
FRANKLIN, R.M.
1912
FRANKS, L.M.
1229, 2099, 2500
FRANTSI, C.
1454
FRANZEN, S.
2531
FRASER, C.F.O.
1059
FRASER, E.E.
1683
FRAUMENI, J.F., JR.
0012, 0808, 1603
FRAYSSINET, C.
0049, 2072
FRAZIER, M.E.
1838
FREEDMAN, M.H.
1237
FREEMAN, A.E.
0953
FREEMAN, A.I.
0694, 2115
FREEMAN, M.A.R.
1853
FREEMAN, R.G.
0536
FREI, J.V.
0088
FREIENSTEIN, C.
0892
FREIENSTEIN, S.
0892
FREIREICH, E.J.
0798
FREMIOTTI, A.
1128

FRETZIN, D.F.
1239
FREYBERGER, H.
1720*
FREZOULS, G.
1438
FRIBERG, L.
0109, 0500
FRIBERG, S.
1445
FRIDLENDER, B.
2561
FRIED, W.
2277
FRIEDEL, G.H.
0976
FRIEDMAN, E.W.
1408*
FRIEDMAN, H.
1022, 1529, 1534,
1535
FRIEDMAN, L.
1275
FRIEDMAN, M.A.
0046
FRIEDMAN, R.M.
2315
FRIEDMANN, T.
0684
FRIEND, C.
0603, 1897, 1898,
2348
FRIESEN, H.G.
1653
FRIIS, R.R.
0640, 1439, 1478,
1479
FRINDEL, E.
1011
FRITSCH, P.
1368
FRITSCH, R.S.
1040
FRONGILLO, R.
2326
FROOMBERG, D.
1636
FRYE, F.L.
2044
FUCCILLO, D.A.
1061
FUCHS, R.
1772
FUERSTENBERG, H.S.
2029
FUGINAGA, K.
0584
FUJII, K.
0958
FUJIMOTO, Y.
1861*
FUJIMURA, S.
2199
FUJINAGA, K.
0143, 0634
FUJINAGA, S.
1938, 2410

FUJIOKA, S.
1950
FUJIWARA, K.
1383
FUKUDA, S.
0489
FUKUNAGA, F.H.
2486
FUKUOKA, F.
0026, 1357
FUKUSHIMA, M.
1983
FULLMER, C.D.
0104
FULTON, D.
0307
FURST, A.
2195, 2268*
FURUKAWA, T.
1121
GABUNIYA, U.A.
0793
GABUTTI, V.
0342*
GADOMSKA, H.
1192*, 1629*
GADRAT, J.
1375*
GAHRTON, G.
2494
GAIDAR, E.I.
0686*
GAIL, M.H.
1500
GAILLARD, J.
0851, 1154
GALBRAITH, P.R.
0290
GALIAN, A.
0371
GALKOVSKAYA, K.F.
1845, 1863*, 1864*
GALL, S.
0787
GALLAGHER, C.H.
0047
GALLAGHER, R.E.
1962
GALLIPPI, G.
2033*
GALLO, R.C.
0790, 0791, 0792,
1204, 1950, 1962,
2089, 2091, 2503
GALTON, D.A.G.
1365
GAMBURG, V.P.
1042
GANE, N.F.C.
1849
GANGADHARAN, P.
2487
GANGAL, S.G.
1072, 1120
GANTT, R.
1200
GANTT, R.R.
2507

GARANCIS, J.
1653
GARAPIN, A.C.
0648, 1081, 1
1941, 1943, 2
GARCIA, F.G.
1059, 1464
GARCIA, H.
0087, 1330
GARDELL, C.
0925
GARDNER, M.B.
1182, 1441, 2
GARFINKEL, H.A.
1830
GARFINKEL, L.
0973, 0974
GARIBYAN, D.K.H.
0443
GARISOAIN, M.J.
0956
GARLAND, M.R.
1770
GARRETT, W.J.
0295*
GART, J.J.
0798
GARTLER, S.M.
1687
GARUSI, G.
0299*
GARVEN, E.V.
2097
GASCOIGNE, R.H.
1616
GASPARINI, C.
1713*, 2577*
GAULDEN, M.E.
1391
GAUTIERI, R.F.
1339
GAVOSTO, F.
0876*, 1281
GAZDAR, A.F.
1443, 1932, 1
GAZZOLO, L.
1481
GEARY, C.P.
0479
GEBHART, E.
0112, 1360
GEDER, L.
1493
GEERING, G.
1975
GEFTER, M.L.
2513
GEISER, J.D.
0339*
GELB, L.D.
2373
GELBOIN, H.V.
0445, 2168*
GELDERBLUM, H.
1909
GELETA, J.N.
1778

LLE, P.
 0747*
 NTIL, A.
 0926
 NTILE, J.M.
 1899
 NTRY, G.A.
 0643
 RARD-MARCHANT, R.
 1371, 1436, 2108
 RBER, P.
 0156, 0576, 1883,
 1884
 REBTZOFF, M.A.
 0469
 RGELY, L.
 0335*, 1445, 1971
 RICKE, D.
 1286, 1551
 RWIN, R.I.
 0589
 Y, G.O.
 1653
 IARPURE, M.
 2327
 MELELOVITCH, S.
 0998
 IACOMETTI, G.
 1506
 BBS, W.N.
 0719
 BEL, W.
 1285
 BLETT, E.R.
 2305
 IBSON, A.A.M.
 1170
 IBSON, R.
 1604
 IBSON, W.
 1069
 IBSON, W.R.
 1287
 IBSON, W.T.
 0196
 IDALI, J.
 2279
 ILBERT, E.F.
 0722
 ILBERT, C.S.
 0283
 ILBERT, F.
 0783
 ILBERT, H.S.
 0320, 0359
 ILBERT HOLLAND, J.
 1897
 ILCHRIST, G.H.
 1237
 ILDEN, R.V.
 0551, 0552, 0555,
 0562, 1070, 2298,
 2318, 2354, 2356,
 2407, 2413, 2457,
 2458
 ILES, A.L., JR.
 0424

GILFILLAN, R.
 0245
 GILLETTE, K.G.
 2129
 GILLIAVOD, H.
 2281
 GILLY, L.
 0135
 GILSON, J.C.
 1610
 GIMMY, J.
 0905
 GINER, J.
 0871*
 GINSEBERG, H.S.
 1913
 GIOVANELLA, B.C.
 0446
 GIRALDO, G.
 1427
 GIRARD, M.M.
 0018*
 GIRARD, R.
 0121*, 1370, 1374,
 GIRARDI, A.J.
 0670
 GIUNTA, J.L.
 1541
 GLAGOV, S.
 1708*
 GLASER, E.M.
 0292
 GLASSER, R.
 1923
 GLAUMANN, H.
 2237
 GLAVINO, J.
 0036
 GLEICH, G.J.
 0724
 GLEICHMANN, E.
 0224
 GLEICHMANN, H.
 0224
 GLICK, M.C.
 1939, 1957
 GLOVER, D.J.
 0940
 GLUCKSMANN, A.
 0441, 0887, 1790
 GMINDER, J.
 1812
 GODARD, C..
 1068
 GODENECHÉ, D.
 0242*
 GODWIN, M.C.
 2257
 GOEHDE, W.
 1722*
 GOELZER, M.L.
 1545
 GOENZCOEL, E.
 1921
 GOERLICH, M.
 1751*, 2223
 GOERTTLER, K.
 0427, 0480, 1349

GOERTZ, E.
 1366
 GOETZ, O.
 0152
 GOFMAN, J.W.
 2095, 2101
 GOGICHADZE, G.K.
 2319
 GOH, K.O.
 1688
 GOLD, P.
 0235, 0358, 2172*
 GOLDBERG, B.I.
 0754
 GOLDBERG, G.M.
 1168
 GOLDBERG, R.J.
 1463
 GOLDBLUM, N.
 2447
 GOLDE, A.
 1078
 GOLDEN, H.D.
 1073
 GOLDENBERG, H.
 1327
 GOLDFEDER, A.
 1842, 2348, 2505
 GOLDIN, A.
 2448
 GOLDMAN, J.M.
 0155, 0246, 2463*
 GOLDMAN, L.I.
 1792
 GOLDMAN, R.L.
 0622
 GOLDSCHMIDT, B.M.
 1291, 2204
 GOLDSTEIN, A.L.
 0197
 GOLDSTEIN, D.H.
 0276
 GOLDSTEIN, G.
 0156
 GOLDSTEIN, M.N.
 1684
 GOLIGHER, J.C.
 1156
 GOLLMAR, Y.
 2397*
 GOLOB, E.
 1261
 GONANO, F.
 2025, 2585*
 GONZALEZ-LICEA, A.
 1714*
 GONZENBACH, P.
 2144*
 GOOD, R.A.
 2401
 GOODALL, C.M.
 0476, 0479
 GOODHEART, C.
 2296
 GOODMAN, M.L.
 2463*
 GOODWIN, F.K.
 1835

GOOR, R.S.
 1953
 GORBACH, P.D.
 1180
 GORBANE, G.P.
 0897
 GORDON, B.S.
 2186
 GORDON, H.L.
 0781, 1429, 1430
 GORLICH, M.
 0007
 GORLING, R.J.
 0244
 GORSKI, T.
 2235
 GOSS, S.G.
 0836
 GOSSEREZ, M.
 1601*
 GOTHOSKAR, B.
 2305
 GOTHOSKAR, S.V.
 0969
 GOTLIEB-STEMATSKY, T.
 1519
 GOTO, S.
 1784
 GOTOH, A.
 0151
 GOUDENAND, M.
 1721*
 GOULD, V.E.
 1378*
 GOUSSEV, A.I.
 2003, 2004
 GOUTIER, R.
 0544
 GOYANES-VILLAESCUSA, V.
 2260
 GRABSTALD, H.
 0114
 GRACE, J.T., JR.
 1882, 1886
 GRADY, L.
 1094
 GRAEF, W.
 1747
 GRAESSMAN, M.
 2077
 GRAESSMANN, A.
 2077
 GRAF, B.
 1410*
 GRAF, T.
 1485
 GRAF, W.
 1333
 GRAFFE, L.H.
 1490, 1498
 GRAFFI, A.
 1426, 1956
 GRAFFI, I.
 1956
 GRAHAM, C.
 1061
 GRAHAM, C.E.
 1158, 1294, 1769, 1804

GRAHL-NIELSEN, G.
 1673
 GRAMMER, F.C.
 0308
 GRAMPA, G.
 1699
 GRANBERG, I.
 1260, 2525
 GRANBOULAN, N.
 1203
 GRANDE, P.
 1630*
 GRANGE, J.
 1949
 GRANOFF, A.
 0189, 2301
 GRANT, G.A.
 0065
 GRANT, R.W.
 0279
 GRANTHAM, P.H.
 0054
 GRAVELL, M.
 0189, 2338
 GRAVES, H.A., JR.
 1711*
 GREEN, H.
 1507
 GREEN, J.W., JR.
 0403
 GREEN, M.
 0143, 0584, 0634,
 1911, 2355
 GREEN, N.M.
 2008
 GREENAWALT, C.
 2376
 GREENBLATT, M.
 0496, 1817, 2241
 GREENE, E.M.
 0785
 GREENWALD, P.
 2019
 GREGORY, J.E.
 0282
 GREGORY, K.F.
 1454
 GREGORY, S.A.
 2582*
 GREY, H.M.
 1127, 1568, 2443
 GRIESEMER, R.A.
 0608
 GRIFFITHS, K.
 0782
 GRIFONI, V.
 0733*
 GRILLI, S.
 1362
 GRIMES, W.J.
 1101
 GRIMLEY, P.M.
 1635
 GRIMM, J.
 0233
 GRIMMER, G.
 0397

GROETENBRIEL, C.
 0981
 GRONMARK, T.
 1164*
 GROPP, A.
 0137
 GROSS, L.
 0351, 0550, 10
 1734
 GROSS, M.
 1168
 GROSSI-PAOLETTI, E.
 0963, 0964
 GROSSMAN, R.A.
 1777
 GROSSO, G.
 2087
 GROUCHY, J.
 0344
 GROUPE, V.
 1472, 1910
 GROVER, P.L.
 0067
 GROVER, S.
 2243
 GRUENSTEIN, M.
 0908, 1327, 17
 GRUENTHAL, D.
 0959
 GRUNBERGER, D.
 2090, 2199
 GRUNDMANN, E.
 1767
 GRUNERT, V.
 1262
 GRUNNET, M.L.
 1196
 GRUPPER, C.
 1516*
 GRYNLAT, A.
 1598*
 GSELL, H.C.
 0577
 GUALANERI, V.
 1284*
 GUARINI, G.
 2021*
 GUBAREVA, A.V.
 1845, 1863*, 1
 GUBERGRITS, M.Y.
 0347
 GUDINSON, D.
 0013
 GUENET, J.L.
 0128
 GUERIN, M.
 0460
 GUEST, G.E.
 1873
 GUETTNER, J.
 1764, 2244
 GUILLE, E.
 0263*, 1254
 GUILLEMAIN, B.
 1068
 GUILLOT, J.
 0242*

MBMANN, M.R.
 0919
 VVEN, P.
 1024, 1973
 NZ, F.W.
 0008, 1206
 RD, J.W.
 2539
 RDA, M.
 2010, 2023*
 RGO, C.
 0143, 0634
 RSEL, E.
 2572
 SSARSKY, J.
 1168
 TMANN, H.R.
 0407, 0876*, 1773
 2183
 DERKEY, F.
 2558
 DERKEY, P.
 2558
 SELEN, A.
 0872*
 AG, D.
 0480, 1349
 AS, M.
 0684
 ER, S.
 1335
 BIBI, A.
 0284, 1179
 CKER, B.
 2309
 DDAD, J.R.
 1898
 OFIELD, E.H.
 0982
 CHAZY, G.
 0335*
 GEMAN, P.
 0627
 SHIGHI, P.
 2488
 GLID, K.G.
 1567
 SMAR, B.
 0078
 GUENAU, F.
 1484
 GUENAUER, J.P.
 0851, 1154
 IN, E.C.
 0214
 IN, E.E.A.
 1524
 IN, G.M.
 2201
 CKEN, B.N.
 1709*
 IN, E.
 2481
 DUKOVIC, S.
 1848
 AMA, M.
 0264, 2117

HAKE, T.
 0226
 HAKOMORI, S.
 1102
 HAKOMORI, S.I.
 2359
 HALAWANI, A.
 0771
 HALDEMANN, R.
 1716*
 HALKETT, J.A.E.
 0225
 HALL, J.G.
 0940
 HALL, W.T.
 1067
 HALLIDAY, W.J.
 1554
 HALPERN, B.C.
 1210
 HALPERN, R.M.
 1210
 HAMAJIMA, K.
 0151
 HAMILTON, P.B.
 0916
 HAMMARSTROM, L.
 1016*
 HAMMER, R.F.
 1877
 HAMMERSTEIN, J.
 0782
 HAMMOND, E.C.
 0973, 0974
 HAMMOND, G.D.
 1237
 HAMMOND, W.G.
 1635
 HAMPAR, B.
 1521
 HAMPEL, K.E.
 1766
 HAMPERL, H.
 2035*
 HAN, T.
 1252
 HANAFUSA, H.
 0204, 1086
 HANAFUSA, T.
 1086
 HANCHARD, B.
 0719
 HANCOCK, R.L.
 2146
 HANES, B.
 1182
 HANING, H.
 0976
 HANNA, C.
 1663
 HANNA, M.G., JR.
 0174, 0609, 2001
 HARA, H.J.
 2162
 HARAN-GHERA, N.
 1325, 1968,
 2434

HARD, G.C.
 0950, 0952, 1807,
 1808, 1809, 2240
 HARDY, R.D.
 2303
 HARDY, W.D.
 2044
 HARDY, W.D., JR.
 1975, 1977
 HARE, J.D.
 1107
 HAREL, J.
 1026, 1438
 HAREL, L.
 1438
 HARKE, H.P.
 1366
 HARMAN, J.W.
 1786
 HARO, R.T.
 2268*
 HARPER, A.
 0268
 HARPER, P.S.
 0776
 HARPER, R.M.J.
 0776
 HARRIS, C.
 0024
 HARRIS, H.
 2386, 2514, 2554
 HARRIS, J.
 1576
 HARRIS, J.W.
 0503
 HARRIS, F.N.
 1287, 1293
 HARRIS, R.
 1141*
 HARRIS, R.J.C.
 0642
 HARROLD, B.
 1073
 HARRY, D.S.
 2548
 HARTENSTEIN, R.
 1350, 1812
 HARTLEY, J.W.
 1115*
 HARTMANN, G.R.
 1572, 1702
 HARTMANN, L.
 2445
 HARTVEIT, F.
 1122
 HARTZELL, R.W.
 0614, 1046
 HARUNA, I.
 0572
 HARVEY, J.J.
 1935
 HARVEY, P.W.
 1256
 HARWOOD, S.E.
 0211
 HASEGAWA, K.
 1515

HASEGAWA, T.
0491
HASHIMOTO, N.
0394
HASHIMOTO, Y.
0055
HASLAM, S.
2349
HATAKEYAMA, S.
0925, 1319
HATANAKA, M.
0204, 0555, 2354
HATANO, T.
1590
HATFIELD, D.
2505
HATFIELD, P.M.
0132
HAUGHTON, G.
1540
HAUNG, A.T.
1542
HAUSE, L.
1653
HAUSE, L.L.
0252
HAVRANKOVA, N.
0768*
HAWKS, A.
2216
HAWKS WORTH, G.
1189
HAWTHORNE, C.
1563
HAY, D.
1895
HAY, J.
0319, 1440
HAYAHARA, N.
2140*
HAYAMI, M.
2446
HAYASHI, H.
0306, 1682
HAYASHI, I.
0511
HAYASHI, K.
1765
HAYASHI, Y.
0491
HAYES, A.
0549
HAYS, E.F.
1035
HEALEY, P.
0499
HEARNE, F.T.
0115
HEARON, E.C.
1512
HEATH, C.M.
0456
HEATH, C.W.
1123, 2535
HEATH, C.W., JR.
0266, 2096
HEATH, J.C.
1853

HECHT, F.
1570
HECKER, E.
0447, 0516*
HEIDBREDE, G.
1182
HEIDELBERGER, C.
0400, 0446, 2221
HEILBRON, D.
1483
HEILMANN, H.P.
0995
HEILPERN, P.
2262
HEINE, U.
1413, 2302
HEISE, E.
2223
HELE, P.
1205
HELLENBROICH, D.O.
0959
HELLMAN, K.B.
0663
HEMPEL, H.C.
0233
HEMPELMANN, L.H.
0138*, 2283
HEMS, G.
0265, 0314, 1250
HENDERSON, E.S.
0798
HENDERSON, J.W.
1149
HENDRY, J.H.
1380
HENLE, G.
0574, 1024, 1025,
1973
HENLE, W.
0574, 1024, 1025,
1973
HENNEKEUSER, H.H.
0137
HENNINGS, H.
0074, 1216, 2059
HENRY, C.J.
2330
HENRY, P.H.
0209, 2332, 2371
HENZELL, S.
1229
HERBER, L.
0266
HERBERMAN, R.B.
1520, 1531
HERBST, A.L.
1831
HERMANUTZ, D.
1010
HERNANDEZ, F.
0960
HEROLD, H.J.
0285
HERRANEN, A.
1219
HERRERA, F.
1204

HERRINGTON, J.L.,
1711*
HERROLD, K.MCD.
0482
HERSH, E.
1576
HERTZ, R.
2076
HERZBERG, M.
1103
HESS, F.
2573*
HESTON, W.E.
0631, 1067,
1695
HEUSON, J.C.
0450, 0930,
HEYDENRICH, M.
0564
HEYDER, J.
1403*
HEY-FERGUSON, A.
1341
HEYN, R.
0310
HIASA, Y.
0430, 1312
HIBBERD, A.D.
2404
HIDASI, G.
0178
HIERHOLZER, J.C.
1054
HIGGINS, M.
1535
HIGGINSON, J.
0377*
HIJMAN, W.
0713
HILDEBRAND, J.
2563
HILDEMAN, W.H.
1986, 2442
HILF, R.
1327, 2222
HILFRICH, J.
2245
HILGERS, J.
2453
HILL, M.J.
1189
HILLCOAT, B.L.
1646
HILLEMANN, M.R.
1961
HILLMAN, E.A.
0580
HILLSTROM, L.
0997
HILSCHMANN, N.
1581*
HINDRINGER, B.
1382
HINRICHS, D.J.
1324
HINTON, R.H.
1636

JUMA, Y.
 1020
 Z, I.
 2481
 ZE, H.C.
 2379
 AI, K.
 1954
 AMATSU, T.
 0511
 ANO, M.
 1560
 AYAMA, T.
 0151
 ONO, I.
 0895, 1765, 2490
 ONO, Y.
 0539
 SCHHORN, K.
 0150
 SCHMAN, S.Z.
 1733
 SHAUT, Y.
 0154, 1023, 1427,
 1435
 ST, J.W.
 1568
 ZANEK, I.
 0581, 1486
 H.C.
 0625
 J.K.
 1111
 GLAND, H.C.
 1147
 BS, C.H.
 1013, 1014, 1015
 BS, J.R.
 0729*, 1737
 H-LIGETI, C.
 2192
 I.
 1411, 1930
 FFEL, J.C.
 1601*
 FFINGER, J.P.
 0411
 GLUND, S.
 0613
 RNI, B.
 0019*, 0354
 FBRAND, A.V.
 0698, 0701
 FMANN, D.
 0977, 2224, 2260
 GAN, M.D.
 0179, 1056
 AMA, A.
 1983
 AMA, Y.
 0324
 E, C.
 2283
 DEN, H.T.
 2436
 OSWORTH, R.N.
 1252

HOLGERSEN, L.O.
 1591
 HOLIK, F.
 0229
 HOLLAND, J.C.
 2213
 HOLLAND, J.M.
 0885
 HOLLEG, A.I.
 1602
 HOLLEY, R.W.
 0217
 HOLLIS, V.W., JR.
 2409
 HOLMES, E.C.
 1536, 1984, 1985
 HOLMSTROM, T.
 0303*
 HOLOWCZAK, J.A.
 2329
 HOLSMAN, J.
 0961
 HOLSTO, L.R.
 1002
 HOMBURGER, F.
 1795
 HONDA, Y.
 1202
 HOOGHE, R.
 0187
 HOPFNER, C.
 0128
 HOPKINS, M.S.
 1099
 HORAK, J.
 2536
 HORCAJADA, J.
 1262
 HORIO, T.
 0035
 HORIN, D.
 0017
 HORN, K.H.
 2238
 HORN, M.
 1764
 HORNE, C.H.W.
 2145*
 HOROSZEWICZ, J.S.
 1882, 2307
 HOROSZEWICZ, S.J.
 1433
 HOSHINO, H.
 0026
 HOSHINO, J.
 2427
 HOSHINO, K.
 1665
 HOSHINO, T.
 0797, 1398, 1399
 HOSHIZAKI, H.
 0509
 HOSOKAWA, M.
 1533
 HOSSFELD, D.K.
 1235, 1252, 1730,
 2175*

HOTTIER, D.
 2432
 HOWARD, A.
 1380
 HOWARD, B.V.
 1502
 HOWARD, E.
 2125
 HOWARD, E.P.
 1838, 1841
 HOWARD, R.J.
 0682*
 HOWARTH, J.L.
 1001
 HOWEL-EVANS, A.W.
 0776
 HOYER, B.H.
 1884
 HOYER, I.
 0773
 HRABOSKA, M.
 1664
 HRUBA, Z.
 2496, 2545
 HSIUNG, G.D.
 1920, 2335
 HSU, C.C.S.
 1574
 HSU, K.C.
 1521
 HSU, L.Y.
 0150
 HU, F.
 0012
 HUANG, C.C.
 2307
 HUANG, E.S.
 2369
 HUANG, L.H.
 1234
 HUANG, S.N.
 1118
 HUANG, W.Y.
 1653
 HUBER, C.
 2584*
 HUBER, H.
 2584*
 HUBERMAN, E.
 2221
 HUDSON, J.B.
 2383, 2392*
 HUDSON, W.R.
 0373
 HUEBNER, G.
 2163
 HUEBNER, R.
 1871
 HUEBNER, R.J.
 0551, 0552, 0555,
 0562, 0597, 1034,
 1070, 1182, 1326,
 1888, 1977, 2298,
 2356, 2376, 2407,
 2413, 2458
 HUGGINS, C.
 0738

HUGHES, L.E.
0454
HUGHES, N.R.
1569, 2419
HUGHES, R.G.
2400*
HUGOSON, G.
2130
HUHN, D.
2020*
HUHTI, E.
0510
HUI, Y.H.
2191
HUIKKO, M.
0510
HULKA, B.S.
1620
HULL, E.W.
0154, 0724
HULTIN, T.
2151
HUME, D.M.
0693
HUMPHREY, R.M.
2250
HUNG, P.
1085
HUNG, I.P.
1482
HUNT, R.C.
1059, 1464, 1917
HUNTER, E.
2391
HURLBURT, J.F.
1857
HURST, L.
0433, 1313
HUSEBY, R.A.
0022
HYDOVITZ, J.
1710*
HYODO, M.
2546
ICHIMAFU, Y.
1398, 1399
ICHIMURA, H.
1826
IDA, N.
1905
IGAKI, I.
1826
II, Y.
0267
IKAWA, Y.
1905, 1937
IKUTA, F.
1255
IL'NITSKLY, A.P.
0515*
IMAI, H.
0261
IMAI, H.T.
0102, 0716
IMAI, T.
2489
IMAMURA, A.
0472

IMAMURA, N.
0092, 0604
IMAMURA, T.
1432
IMASHUKU, S.
2064
IMBENOTTE, J.
1026
INCH, W.R.
1675, 1998
INDGIN, S.N.
0134
INGALLS, T.H.
1219
INOUE, M.
0153
INOUE, T.
0271
INSTITORIS, L.
0422
IOACHIM, H.L.
1449, 1865
IONESCU-HOMORICEANU, S.
1490, 1498
IRISH, L.E.
1324
IRIYA, K.
0511
IRLIN, I.S.
1038, 2194, 2323,
2389
IRVING, C.C.
1298, 1301
ISAKA, H.
0097
ISBRANDT, R.
0924
ISENBERG, I.
0410
ISHIBASHI, A.
2106
ISHIBASHI, Y.
1231
ISHIDA, K.
0267, 1172
ISHIDATE, M.
0093
ISHIKAWA, M.
0511
ISHIKAWA, S.
0322
ISHIKAWA, Y.
1983
ISHIMARU, T.
0267, 1398, 1399
ISHIMOTO, A.
0658
ISHIZAKI, P.
1437, 1890
ISOK, M.E.
1814
ISRAELS, W.C.G.
0717
ITANI, S.
0797
ITO, M.
0040

ITO, N.
0430, 1312
ITO, T.
1839, 1840
ITO, Y.
0151, 0570,
1074, 2381
ITZE, L.
0492
IUDICELLO, P.
2021*
IVANKOVIC, S.
0032, 0090,
0483, 0905,
IVANOV, I.I.
0852
IVASKOVA, E.
0227
IVERSEN, O.H.
0074
IVERSON, U.
0074
IWA, N.
1030
IWAMOTO, K.
0624
IWATA, A.
1511
IZAWA, M.
1658
JABLON, S.
0540
JACKSON, C.D.
1298
JACKSON, E.W.
2133
JACKSON, J.
0203, 0645,
1088, 1483,
JACKSON, J.F.
0807
JACKSON, J.L.
1143
JACKSON, S.
0069
JACKSON, T.A.
1843
JACOB, A.
2214
JACOB, R.M.
2021*
JACOBS, W.H.
0722
JACOX, H.W.
0133
JACQUEMONT, B.
1949
JACQUIGNON, P.
0411, 2269*
JAENISCH, R.
2378
JAFFE, D.N.
2006
JAGATIC, J.
2257
JAHLES, W.G.
1480

INCHILL, J.L.
 0199
 ITLY, S.B.
 1763
 KOBSSON, P.
 0262*
 KOUSSKOVA, J.
 0227
 MDAR, S.C.
 0288
 NIS, R.
 2017
 NISCH, W.
 0965
 NNERS, H.Y.
 2050, 2499
 NOFF, A.
 0059, 0396
 NOWER, M.L.
 1396
 NSEN, E.
 0270
 NZEN, H.A.
 1661
 O, W.
 1239
 RRETT, O.
 0389*, 1440, 1895
 STY, V.
 0182, 0208, 1459
 YLE, M.F.
 1313
 E, W.S.S.
 1003
 HN, U.W.
 0230
 LIU, G.
 0755
 NEY, A., JR.
 0422
 NEY, E.
 1493
 NKINS, D.
 1253
 NNINGS, E.H.
 2180, 2182
 NNISSSEN, H.
 2427
 NSEN, E.M.
 0175, 0626, 0630,
 1420, 1925
 NSEN, K.B.
 0794
 NSEN, M.K.
 0030, 1146
 NSEN, R.
 0525
 NSEN, R.D.
 0808
 NSON, A.B.
 2565
 REB, B.
 2015
 LDEROS, B.
 1645
 NG, B.S.
 0535

JOBBARD, P.
 2111
 JOHANSSON, B.
 1025
 JOHANSSON, G.
 0462
 JOHNSEN, D.O.
 1777
 JOHNSON, A.D.
 0133
 JOHNSON, D.F.
 0994
 JOHNSON, E.M., JR.
 2064
 JOHNSON, G.S.
 2315
 JOHNSON, L.I.
 0391*
 JOHNSON, P.M.
 0124
 JOHNSON, T.
 0678
 JOHNSON, W.C.
 1860
 JOHNSTON, B.
 0340*
 JOHNSTONE, C.
 2012
 JONAS, A.M.
 1461, 2502
 JONDORF, W.R.
 1346
 JONES, D.
 0782
 JONES, D.S.
 1683
 JONES, E.E.
 1548
 JONES, H.W., JR.
 0254
 JONES, K.P.
 2203
 JONES, N.D.
 1644
 JONES, R.K.
 1013, 1014, 1015
 JONSSON, N.
 0656
 JOSE, D.G.
 2401
 JOSEPH, W.L.
 0695, 0704
 JOSEY, W.E.
 0185
 JOSHI, V.V.
 0088
 JOURNEY, L.J.
 2115
 JOYET, G.
 1400
 JUJCHAU, M.R.
 1799
 JUDD, K.P.
 2431
 JUHL, E.
 2102
 JUMINER, B.
 1727

JUNGSTAND, W.
 1764, 2244
 JUSSAWALLA, D.J.
 1177, 2042
 JUSTUS, J.
 2185
 KABAKOV, Y.N.
 0534
 KACHI, H.
 2490
 KADACH, D.
 1135
 KADIN, M.E.
 1704
 KAESER, H.
 1242, 2587*
 KAFUKO, G.W.
 0006
 KAHL, G.F.
 0188
 KAJI, H.
 0170, 1533
 KAKEFUDA, T.
 2332, 2392*
 KAKIZAWA, H.
 1560
 KALIEV, J.
 0671
 KALLNER, H.
 1615
 KAMADA, N.
 0541
 KAMBOJ, V.P.
 0689
 KAMINSKAYA, L.P.
 0943
 KANAMAKU, R.
 0490
 KANAPILLY, G.M.
 1013
 KANG, H.S.
 1504
 KANPFSKY, P.
 1221
 KAPLAN, M.M.
 0246
 KAPLAN, P.M.
 1457, 2449
 KAPLOW, L.S.
 1920
 KAPULER, A.M.
 1774
 KAR, A.B.
 0869, 0985
 KARA, J.
 0676
 KARASAKI, S.
 2061
 KARAZAS, V.
 0675
 KAREWICZ, Z.
 1192*, 1629*
 KARKUN, J.N.
 0985
 KARL, S.
 2456
 KARNAUKHOVA, E.N.
 2219

KARSTEN, C.
0904
KASAHARA, A.
0509
KASHA, M.
0345
KASHIMA, M.
2284
KASILI, E.G.
1166
KASPER, C.B.
0913
KASUGA, T.
2106
KATAGIRI, M.
0322
KATAGIRI, S.
1020
KATCHALSKI, E.
0236, 0661, 1377*
KATO, H.
0540, 1172
KATO, N.
1784
KATO, R.
0093, 0967
KATO, S.
1028, 1029, 1030,
1063, 2380, 2393*
KATO, T.
1861*, 2490
KATSUKI, H.
0096
KATZ, C.
1291, 2204
KAUFMAN, L.
0083
KAUFMAN, R.H.
0744
KAUFMAN, R.J.
0785
KAUFMANN, L.A.
0620
KAUL, A.
1403*
KAWAKAMI, H.
1087
KAWAKAMI, T.G.
1874
KAWAMURA, A., JR.
0151, 1972
KAWAMURA, M.
2546
KAWASAKI, S.
0797
KAWASHIMA, K.
0093, 1560, 1658
KAWAZOE, Y.
1356, 1358
KAY, S.
0693, 2195
KAZANOVA, L.I.
1596
KAZANTSEVA, I.A.
2468
KEARNEY, R.
0454

KEARNS, F.
1798
KEAST, D.
2316
KEDAR, E.
2447
KEEBLER, C.M.
2045
KEEFER, L.
0087
KEEN, P.
1781
KEENEY, A.H.
1234
KEIDITSCH, E.
1649
KEITH, L.
0364, 0365, 0861
KELEMEN, E.
2273*
KELLEN, J.A.
0932, 1990
KELLER, J.M.
0002
KELLER, R.
2118
KELLOFF, G.
0551, 0552, 2354,
2457, 2458
KELLOFF, G.J.
0562
KELLY, F.
0484
KENNEY, F.T.
2551
KENYON, A.J.
1644
KEOWN, D.
1211
KEPLINGER, M.
0421
KERCKAERT, J.P.
0495
KEPR, H.A.
0063
KERR, J.F.R.
0795
KERR, S.J.
2511
KERTSMAN, V.I.
2161
KESSLER, I.I.
1724
KETCHAM, A.S.
0704
KETTERER, B.
1315
KEVIN, D.M.
0860
KEYDAR, J.
0141, 0142, 0, 53
KHALATBARI, A.
2578*
KHAN, A.U.
0345
KHOKHLOVA, M.P.
2046

KHOLMUKHAMEDOVA, N.M.
1048, 2333
KHOOBYARIAN, N.
0181
KHOR, H.T.
0062
KHUDOLEY, Y.V.
2167*
KHUNDANOVA, L.L.
0434, 2423
KIEFER, G.
1775
KIEFF, E.D.
2310
KIELER, J.
2420
KIESSLING, A.A.
1892, 1893, 208
KILLMANN, S.A.
1686
KIM, C.A.H.
1553
KIM, C.S.
1817
KIM, S.N.
1644
KIM, U.
2275
KIMMEL, CH.B.
2450
KIMUKA, I.
0658
KIMUKA, M.
1810
KINARD, R.
0003
KING, C.M.
1306
KING, D.
2201
KING, L.R.
1143
KING, F.J.
0338*, 0834
KINGSBURY, D.W.
0176
KINT, A.
0862*
KINZEL, V.
0408, 0447, 08
KIPLING, M.D.
0859
KIPP, W.H.
0029
KIRIMOTO, K.
1217
KIRMAN, D.
0973, 0974
KIRN, A.
0522
KIRSCH, M.
0936
KIRSCH, W.M.
1698
KIRSCHSTEIN, R.L.
2341
KIRSNER, J.B.
0528, 1708*

IERSON, U.E.
 0347
 IERSTEN, W.H.
 1108, 1936
 IERTANE, J.S.
 2038
 IERZEDER, H.
 0966
 IERSELEV, F.L.
 1038
 IT, S.
 0664, 0666, 1503,
 1951
 ITAGAWA, T.
 1784
 ITAMURA, H.
 0571
 ITANO, Y.
 0812
 ITTLICK, P.D.
 0084
 IVILAAKSO, E.
 0901, 2070
 LASSEN, A.
 0059, 0398
 LAUBER, M.R.
 0278
 LEHR, H.U.
 1231
 LEIHUES, P.
 2249
 LEIN, E.
 1445
 LEIN, G.
 0153, 0574, 0578,
 0579, 0841, 1024,
 1025, 1121, 1739,
 1971, 1973, 2158,
 2305, 2386, 2514,
 2554
 LEIN, H.J.
 2163
 LEIN, K.M.
 1303
 LEIN, M.G.
 1859
 LEINSASSER, O.
 2163
 LEITKE, CH.
 2223
 LIETMANN, W.
 1537
 LINGE, O.
 2073
 LINGMULLER, G.
 1231
 LOBUSICKA, M.
 2429
 LOPFER, U.
 2013
 LOTZ, H.P.
 2173*
 LUBES, P.
 1346
 MET, J.
 0857
 NAPP, D.R.
 0863*

KNEDEL, M.
 0966
 KNIGHT, C.A.
 0148
 KNIGHT, S.C.
 1996
 KNOECHELMANN, R.
 0765*
 KNOFF, P.M.
 1667
 KNORRE, D.
 0898
 KNOSPE, W.H.
 2582*
 KNOTH, M.
 1653
 KNOW, W.E.
 0288
 KNOWLES, J.C.
 1300
 KNUITSEN, T.
 0576, 0798, 1512
 KNYSZYNSKI, A.
 1657
 KOBAYASHI, H.
 0170, 1533, 2411
 KOBAYASHI, J.
 1389, 1390
 KOBAYASHI, N.
 0096, 1121
 KOBAYASHI, S.
 0528
 KOCH, M.A.
 1497
 KODAMA, M.
 2366
 KODAMA, T.
 0561
 KOERDLER, J.
 1633*
 KOETHE, W.
 1593
 KOETSAWANG, A.
 1706
 KOETSAWANG, S.
 1706
 KOFLEK, W.
 1692
 KOGAN, B.
 1182
 KOGAN, I.YA.
 1048
 KOH, J.K.
 0674
 KOHEN, M.
 1577
 KOHLER, D.E.
 0163
 KOHNE, D.E.
 2373
 KOHONEN, A.
 0530
 KOHSE, L.M.
 2392*
 KOIZUMI, J.
 2104
 KOJIKAWA, M.
 1963

KOLDOVSKY, F.
 0669
 KOLEV, K.
 0996
 KOLODNY, E.H.
 0568
 KOLODZIEJSKA, H.
 1167
 KOLOUSEK, J.
 0405
 KOMABA, M.
 1983
 KOMMIJEMI, V.R.C.
 0496
 KONDRATICK, J.
 2302
 KONIKOVA, E.
 2429
 KONISHI, Y.
 0430
 KOHO, S.
 2140*
 KONOBE, T.
 1029
 KONRAD, K.
 1368
 KONSTANTINOV, V.G.
 2259
 KOO, G.C.
 1529, 1535
 KOPPER, L.
 0816
 KOPROWSKI, H.
 0669, 1092, 1931
 KORB, J.
 1837*
 KOREN, H.S.
 2057
 KORENEVSKAYA, M.I.
 2574*
 KORNITSKY, M.A.
 1329
 KOROL, W.
 0175, 1925
 KOROSTELEVA, T.A.
 0732*, 0911
 KOSEK, J.C.
 0131
 KOSHIBA, K.
 0094
 KOSIOROWSKA, J.
 1415
 KOSLOWSKI, L.
 0139*
 KOSS, L.G.
 1302, 1304
 KOSUT, V.
 2484
 KOSZAROWSKI, T.
 1192*
 KOTLER, M.
 0636
 KOTTARIDIS, S.D.
 1466
 KOTULOVA, D.
 2274
 KOURI, R.E.
 2229

KOVACS, K.
0438, 0925, 1319,
2217, 2227
KOWALEWSKI, K.
1347
KOWALSKI, R.
2576*
KOZLOWSKI, H.
1664
KRAIN, L.S.
1178, 2479
KRAISFLBURD, E.
2336
KRAKOFF, I.H.
2083
KRAMARSKY, B.
1419, 1926
KRARUP, T.
1787
KRASNYANSKAYA, P.N.
1833, 2196
KRATOCHWIL, A.
2137
KRAWCZYNSKI, K.
1034
KREIBICH, G.
0447, 0516*, 0692
KREIDER, J.W.
1522
KREMER, W.B.
1542
KREN, V.
0706, 0900
KRENOVA, D.
0706, 0900
KREUS, K.E.
2117
KRIEK, E.
2181
KRIPKE, M.
1558
KRIPKE, M.L.
0894, 1530
KRISHNA MURTHY, A.S.
1199
KROEGER, H.
2427
KROGH JENSEN, M.
1686
KROH, H.
1342, 2087
KRSMANOVIC, V.
2071
KRUEGER, C.
0904
KRUEGER, F.W.
0082, 1351, 1762
KRUEGER, G.
1589
KRUEGER, G.R.F.
1539
KRUG, H.
2516
KRUPLEY, J.
0235
KRUSE, H.
0032, 0905.

KRUSH, A.J.
1278, 2533
KRUSTAK, E.
0221*
KRUT'KOVSKAYA, N.P.
2468
KRYUKOVA, I.H.
0654, 2367
KUBELKA, V.
0229
KUBIK, A.
0751
KUBINSKI, H.
0913
KUBO, T.
2489
KUCEROVA, M.
0538
KUCHERIA, K.
0302*, 1230
KUDYNOWSKI, J.
0262*
KUEHNEL, W.
1041
KUEHNERT, M.
1662
KUKAYN, R.A.
1473
KULA, N.S.
2210
KULLMANN, R.
1775
KULP, H.W.
2128
KUMANISHI, T.
0653, 1255
KUMKUMADZHYAN, V.A.
0453
KULOUR, V.
0103
KUNIMOTO-MIYATA, S.
1784
KUNKEL, H.G.
1127
KUNTZMAN, R.
1334, 1335, 1805
KUNZE, E.
2024
KURATSUNE, M.
2202
KURBANOVA, A.
1596
KURIHARA, T.
1826
KURIMURA, T.
1951
KURODA, K.
2207
KUROKI, T.
0098, 0490
KUROYANAGI, T.
0709
KURTH, R.
0856
KURTZ, H.
1431
KUSANO, T.
1507

KUSCHNER, M.
1859
KUSIAK, R.J.
0373
KUTINOVA, L.
1509
KUWABARA, N.
2253
KUWATA, T.
0867*, 1087
KUZMINA, S.V.
1717*
KUZMINYUK, A.I.
2259
KUZNETSOVA, N.N.
0655
KUZNETZOV, O.K.
0560, 1947
KVEDAR, J.P.
2366
KWAN, H.C.
0625
KYLE, R.A.
0266, 0507, 2
LABROSSF, E.H.
2064
LACASSAGNE, A.
0411, 0433, 1
LACHAPELLE, F.L.
1243
LACKNER, A.
1766
LACOUR, F.
0587, 1026, 1
2308
LAFARGE, C.
0049
LAFONT, J.
0991*
LAFONT, P.
0991*
LAFUMA, J.
1410*
LAGEMAN, A.
0965
LAGERLOEF, B.
1889
LAGERON, A.
1780
LAGHI, V.
1690
LAGRUTTA, J.
1585
LAGUENS, R.P.
1585
LAHIRI, B.
1624
LAIRD, C.W.
0802
LAIRD, H.M.
1895
LAKSHMI, M.S.
0293
LALLI, A.
2562
LAM, K.M.
2335

K.W.
 1637
 B, M.J.
 2208
 BERNSON, H.V.
 0191
 M, L.U.
 0794
 PER, F.
 0149
 PERT, F.
 0152
 DO, D.
 1759*
 DON, J.C.
 1872, 1974
 DSCHUETZ, C.
 0032, 0905, 2252,
 2265*
 E, D.
 0136
 E, M.
 0467
 E, W.T.
 0562
 E BROWN, M.M.
 2093
 GE, J.
 0711, 1909, 2312
 LOIS, A.J.
 0580, 1105, 1735,
 1890
 GMAN, M.J.S.
 1228
 ZEROT11, R.
 2005
 ZOLA, E.
 1622
 IS, K.
 0816, 1670
 ORTE, G.
 0354
 PE, M.
 2424
 PE, M.A.
 1530
 SON, C.
 1903
 SON, V.L.
 1877
 SON, V.M.
 1961
 SSON, B.
 1007
 FARGUES, E.Y.
 1419, 1926
 HER, R.
 0567
 KOV, R.
 2005
 NE, C.
 0926
 QUELLEC, F.
 0758, 1476
 M.
 1343
 MOND, J.
 1068

LAURENCE, K.R.
 1208
 LAURENT, M.
 1685
 LAURSEN, B.
 0110
 LAUSCH, R.N.
 1982
 LAVAPPA, K.S.
 1828
 LAVE, L.B.
 0016
 LAVIN, P.
 1302, 1304
 LAVRENT'YEV, L.N.
 2294*
 LAW, L.W.
 1543
 LAWLEY, P.D.
 0485
 LAWRENCE, W.C.
 2337
 LAWSON, T.A.
 0028, 1320
 LAZAR, P.
 0460
 LE BRETON, E.
 0849, 2214
 LE CLERC, J.C.
 0165
 LEDERER, J.
 0879*, 2584*
 LEDINKO, N.
 0210
 LEDLIE, E.M.
 1180
 LEE, A.E.
 1215, 1226
 LEE, A.K.Y.
 1119
 LEE, C.G.
 1049
 LEE, D.J.
 1308
 LEE, J.A.H.
 0835, 1632*
 LEE, J.C.K.
 2550
 LEE, K.J.
 0261
 LEE, K.L.
 2551
 LEE, K.M.
 0163
 LEE, K.T.
 0261
 LEE, K.W.
 0978, 0979
 LEE, K.Y.
 0047
 LEE, L.F.
 1465, 2310
 LEE, P.N.
 1191*
 LEE, R.E.
 2110
 LEE, R.O.
 1211

LEE, S.H.
 0043
 LEE, S.K.
 0261, 1578
 LEE, S.L.
 0150
 LEE, S.Y.
 2071
 LEE, Y.K.
 0551
 LEEC, J.B.
 1965
 LEENE, W.
 0713
 LEFFALL, LAS.D., JR.
 0273
 LEFKOWITZ, S.S.
 1981
 LE FRANCOIS, D.
 2416
 LEGALLAIS, F.Y.
 2306, 2341
 LEGATOR, M.
 0484
 LEGEAY, G.
 0127, 0128
 LEGRAND, E.
 0019*
 LEGROS, H.
 0450, 0930, 1243
 LEHMAN, J.M.
 1089
 LEHMANN, A.R.
 0523
 LEHMANN, H.E.
 1580*
 LEHNER, T.
 1150
 LEHNERT, G.
 0112
 LEHRER, R.I.
 2461
 LEIBOWITZ, U.
 2485
 LEINIKKI, P.
 1755*
 LEJEUNE, F.
 2438
 LEJNEVA, O.M.
 0598
 LEKSELL, L.
 1007
 LELIEVRE, L.
 0819
 LEMERLE, J.
 1371
 LENNARTZ, K.J.
 1720*
 LENNETTE, E.H.
 1447
 LENNOX, E.S.
 1667
 LENTLE, B.C.
 0111
 LEONARD, A.
 1392, 2281, 2524
 LEONE, G.
 0877*

LEONG, B.K.J.
 1761
 LEONG, J.
 1487
 LEONG, J.A.
 1941
 LEONG, J.L.
 0070
 LESHER, J.
 0123
 LESHER, S.
 0123
 LESLIE, G.
 0324
 LEUCHTENBERGER, C.
 0501, 1367
 LEUCHTENBERGER, R.
 0501, 1367
 LEVAN, A.
 1697
 LEVI, M.M.
 2000
 LEVI, P.E.
 1300
 LEVIJ, I.S.
 0449, 0451, 0452
 LEVIN, A.G.
 1140, 1504
 LEVIN, M.J.
 0209, 1052, 2332,
 2371
 LEVINE, A.
 2378
 LEVINE, A.J.
 1952
 LEVINE, A.S.
 0209
 LEVINE, L.
 2069
 LEVINE, P.H.
 1434, 1578
 LEVINE, W.G.
 0458
 LEVINSON, W.
 0203, 1081, 1483,
 1941, 1943, 2357
 LEVINSON, W.E.
 0645, 0646, 0648,
 1088, 1487
 LEVY, C.C.
 2074
 LEVY, J.A.
 0606, 1435, 2350
 LEVY, J.P.
 0165
 LEVY-PINTO, S.
 1188
 LEWIS, A.M., JR.
 1052, 1980, 2332,
 2371
 LEWIS, R.
 1060
 LEWIS, R.T.
 1885
 L'HIRONDEL, A.M.
 1476
 LI, C.P.
 1480

LI, C.Y.
 1637
 LI, F.P.
 0808
 LI, L.H.
 1444
 LIBBY, P.R.
 1791
 LICHTENBERGER, E.
 2035*
 LIEBELT, A.G.
 0467, 2547
 LIEBELT, R.A.
 0467, 2547
 LIEGEL, J.
 0446
 LIJINSKY, W.
 0047, 0086, 0087,
 0476, 0479, 1330,
 2209
 LIKHACHEV, A.YA.
 1816
 LILLEHOJ, E.B.
 0388*
 LILLY, F.
 0197, 1904
 LILLY, L.J.
 2208
 LIMA, J.B.
 2581*
 LIMONTA, A.
 2193
 LIN, P.S.
 1873
 LIN, T.M.
 2491
 LINDAHL-KIESSLING, K.
 0521, 0526
 LINDEMAN, R.D.
 0761
 LINDHOLM, L.
 0526
 LINDNER, J.
 2408, 2433
 LINDSAY, S.
 0789
 LINDSTROM, F.D.
 1139
 LINDUP, R.
 1849
 LING, R.C.
 2557
 LINKER-ISRAELI, M.
 2430
 LINMAN, J.W.
 1147
 LINNIK, A.B.
 2228
 LINSK, J.
 0262*
 LIONS, J.
 1214
 LIOZNER, A.L.
 0057, 0144, 0145
 LIPKIN, M.
 2076
 LIPPINCOTT, B.B.
 0404

LIPPINCOTT, J.A.
 0404
 LIPSCHUTZ, A.
 0385*
 LIS, H.
 0708
 LITWACK, M.
 2518
 LIU, C.H.
 0151
 LIU, W.
 1225
 LIVINGSTON, A.M.
 2120
 LIVINGSTON, V.W.C.
 2119, 2120
 LIZZI, F.F.
 0130
 LLOMBART, A., JR.
 1373*
 LLOYD, J.W.
 1369
 LOCKETT, L.J.
 2486
 LODDO, S.
 0766*
 LOEB, L.A.
 0703
 LOEWEL, K.R.
 2029
 LOFT, H.
 1787
 LOG, T.S.
 2311, 2413
 LOH, A.
 1796
 LOHS, KH.
 2187
 LOMAKIN, M.S.
 0455
 LONAI, V.
 0893
 LONBERG-HOLM, K.
 0613
 LONDON, W.T.
 1061
 LOONEY, W.B.
 2050, 2499
 LOOS, J.A.
 1137
 LOOSLI, C.G.
 1182
 LORAS, B.
 1642
 LORENC, R.
 1654
 LORENZ, D.E.
 2341
 LOTLIKAR, P.D.
 0906, 0909
 LOUIS, C.J.
 0053
 LOUIS, J.B.
 1825
 LOURIA, D.B.
 1776
 LOUSSOUARN, J.
 2031*

TIT, J.F.
 0001, 1381
 E, C.R.
 1187
 AND, R.
 1757*
 ET, R.A.
 2229
 ETZKI, J.
 1279
 AS, H.F., JR.
 1006
 CA, A.
 2055*
 E, C.F.
 1185
 IAK, M.
 1600*
 OW, A.
 0216
 WIG, G.
 1041
 WIG, H.
 1881
 DERS, G.
 1227
 INBUHL, R.E.
 1466
 PFOLD, H.E.
 2203
 G.S.
 0559, 1412, 1424
 OBERG, S.
 1190*
 DIN, F.E.
 2480
 DIN, F.E., JR.
 0297*
 OMAN, T.
 0109
 OU, M.
 2365
 E, M.
 1325
 HRA, U.K.
 1624
 A.
 1382
 AN, J.T.
 0539
 CH, H.T.
 1278, 2533
 CH, T.P., JR.
 2068
 N, T.N.
 0796
 N, G.
 1484
 ENKO, N.I.
 0686*
 E, C.D.
 0663
 G, T.A.
 2309
 GS, H.
 0959
 UCHI, K.
 0286

MACA, R.A.
 1413
 MACBETH, R.G.
 0982
 MAC DONALD, J.B.
 1228
 MAC DONALD, W.E.
 0421
 MACEK, M.
 1693, 1885
 MAC FARLAND, H.N.
 1761
 MACHALA, O.
 0201
 MACHLEDER, H.
 0014
 MAC INTOSH, I.J.C.
 0527
 MACKAY, B.
 1161
 MACKAY, I.R.
 1119
 MACKOVA, V.
 1693
 MAC MAHON, B.
 0260, 1187, 1618,
 2491
 MAC MAHON, C.E.
 1395
 MAC MANUS, J.P.
 0818
 MAC MILLAN, D.S.
 2093
 MAC PHERSON, I.
 0390*, 1514
 MAC PHERSON, I.A.
 2155, 2361, 2477
 MADON, E.
 2021*
 MAEDA, T.
 0416
 MAEDA, Y.Y.
 1583*
 MAENO, H.
 0305
 MAENPAA, P.H.
 2475
 MAGEE, P.N.
 0473, 0954, 061,
 1820, 2150
 MAGGI, V.
 0337*
 MAGILNER, L.
 1221
 MAGUDA, T.A.
 0316
 MAHALEY, M.S., JR.
 2016
 MAHER, B.C.
 1474, 1894
 MAHI, P.N.
 1624
 MAIR, A.
 1170
 MAIR, W.
 1007
 MAIROSE, U.B.
 1613

MAISIN, J.R.
 1009
 MAJOK, I.R.
 1806
 MAJSKY, A.
 0227
 MAJUMBAR, S.K.
 0661, 1340
 MAK, S.
 0611, 1914
 MAKAROVA, G.F.
 2389
 MAKAVEEVA, V.
 0652
 MAKINO, S.
 0234, 1224
 MAKKAVEYEVA, M.YU.
 0763
 MALAK, C.
 0294*
 MALAMUD, D.
 1674
 MALAN, L.
 1434
 MALAN, L.B.
 1974
 MALATHI, V.G.
 1901
 MALAYIYA, B.
 0985
 MALEJKA-GIGANTI, D.
 2103
 MALHOTRA, S.L.
 1597
 MALL, .
 0750
 MALLEIN, M.L.
 1374*
 MALLING, H.V.
 0855
 MALMGREN, R.A.
 1539, 1880
 MALMQUIST, W.A.
 0563, 1875
 MALT, R.A.
 1674
 MALY, V.
 0768*
 MANAKER, B.A.
 1413
 MANASTER, J.
 1223
 MANCINI, L.O.
 0182, 0208, 1459
 MANCONI, P.E.
 0733*
 MANCUSO, T.F.
 0300*
 MANDEL, L.R.
 2309
 MANDEL, M.A.
 0691
 MANDY, S.H.
 0134
 MANGI, R.J.
 0237
 MANGUM, J.H.
 1496

MANILDI, E.R.
0788
MANKOWSKI, Z.T.
1801
MANLY, K.F.
1446
MANN, D.E., JR.
1339
MANN, J.
2336
MANN, J.R.
2060
MANNERING, G.J.
0464, 1344
MANNING, M.D.
1603
MANOCHA, S.L.
1294, 1769
MANOJLOVIC, N.
0936
MANOLOV, G.
1697
MANSELL, P.W.A.
1423
MANTANI, M.
2380, 2393*
MANTOVANI, G.
0733*
MANZKE, E.
1862*
MARCUS, D.M.
2017
MARCUS, N.
1598*
MARDINEY, M.R., JR.
0237
MARIANO, M.
0329
MARINARI, U.M.
0122*
MARINI, M.
2025
MARINONI, A.
1622
MARK, J.
0804, 0805, 1084,
1260, 2092, 2519,
2525
MARKEWITZ, M.
2535
MARKHAM, P.D.
1942
MARKUN, F.
1006
MARMOR, J.
2518
MARQUARDT, H.
0058, 0412, 2218,
2224
MARROQUIN, F.
0406
MARSHAK, R.R.
1876, 2012, 2128
MARSHALL, K.G.
1118
MARTANI, A.
2269*

MARTEN, M.A.
2373
MARTENS, J.G.
2012
MARTIN, G.S.
0202, 0205
MARTIN, J.E.
2012
MARTIN, M.A.
1090, 1095
MARTIN, P.
1781
MARTINEZ DE MORENTIN, J.
0960
MARTINEZ-MANAUTAU, J.
0671*
MARTYNOVA, R.P.
0826*
MARUYAMA, K.
2295
MARUYAMA, Y.
0223, 1976, 2289
MARYLANDER, H.
1182
MASEK, V.
1800
MASERA, P.
0342*, 0876*
MASHEVSKIY, A.A.
0763
MASON, M.M.
0146, 0626, 1420
MASSEYEFF, P.
2004
MASSICOT, J.
1036
MASSICOT, J.G.
0171
MASSIMO, L.
0099
MASUDA, S.
0416
MASULA, Y.
2202
MASUJI, H.
0098
MATALKA, E.
1259
MATHE, G.
2108
MATHIESON, B.J.
0590
MATHISEN, W.
0828*
MATOVINOVIC, J.
2562
MATSUBARA, S.
1008
MATSUMOTO, T.
0056, 0432
MATSUOKA, O.
2284
MATSUYA, Y.
1241
MATSUYAMA, M.
0498, 1354, 1429
MATSUZAWA, A.
0633

MATSUZAWA, T.
2282
MATTELIN, G.
2496
MATTINGLY, R.F.
0252, 1653
MATUA, Y.
0035
MATVEYCHUK, YA.D.
1794
MAUDERLY, J.L.
1013
MAUL, G.G.
0786
MAURER, B.A.
1432
MAURER, L.H.
0508
MAWDESLEY-THOMAS,
0499
MAXFIELD, W.S.
1295
MAXWELL, K.W.
2261
MAYFIELD, E.D., JR.
2547
MAYO, A.A.
2050, 2499
MAYS, C.W.
1000, 1003
MAZURENKO, N.P.
0595, 2319
MAZUROVA, N.
1415
MC ADAM, W.A.F.
1156
MC ALLISTER, R.M.
2298
MC BRIDE, R.A.
0050
MC BRIDE, R.Z.
1317
MC CALL, M.G.
2049
MC CARTER, J.A.
1896, 2225
MC CLANAHAN, M.S.
0179
MC CLELLAN, R.O.
1013, 1014, 1
MC COLLESTER, D.L.
1549
MC CORMICK, K.J.
1417, 2343
MC COY, J.
1936
MC CREDIE, J.A.
1675, 1998
MC DONALD, A.D.
0268
MC DONALD, J.C.
0268
MC DONALD, S.
2327
MC DONNELL, J.
1943
MC DONNELL, J.P.
0648, 1081

DONOUGH, S.K.
1975, 2044
DOUGALL, P.T.
0617
EWEN, J.
1170
FARLAND, V.W.
0568
FARLANE, E.S.
1049
FARLANE, H.
0573
FEE, A.F.
1005
GOVERN, V.J.
2093
GRATH, H.
2553
GRATH, L.
2392*
GREGOR, D.H.
1172
HUGH, R.B.
0223
INTYRE, N.
2548
INTYRE, O.R.
0508
KINLEY, T.W., Jr.
0533
KINNELL, R.G.
0896
KINNIE, K.L.
2557
KISSICK, G.E.
0608
LEAN, A.E.M.
0954
MILLAN, M.
2103
MILLAN, V.L.
2449
QUARRIE, H.G.
0503
REYNOLDS, D.G.
1518*
DE, H.M.
0191
INA, A.
0821
INA, D.
0076, 1789, 1802
RAS, K.
2190
ZIHRADESKY, J.
2429
SE, D.
0135
GITT, B.F.
0338*
ITA, F.S.
0247
ER, H.
0562, 0597, 0802
NS, F., JR.
1694
TES, J.
0440, 0770, 0929

MEKLER, L.S.
0207
MELCHERS, F.
0720, 1565
MELCHIONNE, S.
1291, 2204
MELENDEZ, L.V.
0619, 1057, 1059,
1464, 1917, 1918,
1919
MELEWICZ, F.
0695
MELLEGREN, J.
2052
MELLON, J.G.
2050, 2499
MELLOR, J.E.
1206
MELLORS, R.C.
1034
MELNICK, J.L.
0624, 1455, 1457,
1924
MELONI, G.A.
1517*
MENDEZ, W.M.
0297*, 2480
MENEZES, J.
1955
MENYE, P.A.
1266*
MERANZE, D.R.
1327, 1792
MERANZE, R.D.
2495
MERGENHAGEN, S.E.
0882*
MERKER, H.
1753*
MERKOW, L.P.
1296, 2330
MERLER, E.
1647
MERLIE, K.
0775
MERRICK, S.
2425
MERRILL, J.M.
0835
MESROBIAN, A.Z.
1788
MESSER, J.
1821, 1991
MESSERSCHMIDT, O.
0139*
MESSINETTI, S.
2586*
METCALF, D.
0599, 2404
METTLER, N.E.
1995
METZGAR, R.S.
1542
METZLER, M.
0031, 0412
MEUNIER, M.
0921, 0923

MEYER, G.
0241*, 2437
MEYER-BERTENRATH, J.G.
0475
MEYERS, P.
1964, 2436
MEYLER, L.
0506
MICHALK, D.V.
0427
MICHEL, H.
1643
MICHEL, I.
1327
MICHELSON, A.M.
1774
MICKEY, M.R.
0120*
MIDDLETON, C.A.
0714
MIDDLETON, V.L.
0714
MIDDLETON, W.R.J.
0740
MIETTINEN, O.S.
0260, 1396
MIGLIORE, P.
1576
MIHAILOVICH, N.
0492, 0496, 0497
MIKAMI, T.
0159
MIKAT, B.
0765*
MIKULIK, F.M.
1969
MIKUNI, C.
0234, 1224
MIKUNI, M.
0322
MILES, E.M.
0318
MILLER, R.A.
1431
MILLER, D.
2463*
MILLER, D.G.
1140
MILLER, D.R.
1709*
MILLER, E.C.
1827
MILLER, E.S.
2085
MILLER, G.
1021
MILLER, J.A.
1827
MILLER, J.M.
2129
MILLER, L.D.
2129
MILLER, L.T.
1459
MILLER, M.H.
1021
MILLER, R.E.
1591

MILLER, R.W.
1606
MILLMAN, P.A.
1661
MILNE, J.E.H.
0116
MINEI, S.
2104
MINEKAWA, Y.
1044
MINET, P.
0469
MINKLER, J.L.
2095, 2101
MINOWADA, J.
0571, 2307
MINTON, J.P.
0662
MIRA, E.
0251
MIRAND, E.A.
1902
MIROFF, G.
0191
MIRONESCU, S.
1297, 1491
MIRRA, A.P.
1187, 1618
MIRVISH, S.S.
0083, 2241
MISFELDT, C.S.
1144
MISHIMA, Y.
0846
MISTRY, P.B.
0592, 0999
MITAL, V.P.
1624
MITCHELL, G.W., JR.
0245
MITELMAN, F.
1004
MITTELMAN, A.
2520
MITUS, W.C.
1603
MIURA, M.
1560
MIWA, K.
2251
MIWA, T.
1765
MIYAGI, K.
1702
MIYAKE, T.
0658
MIYAMOTO, K.
1521, 2318
MIYAMOTO, T.
1086
MIZELL, M.
0621, 2340
MIZUKAMI, T.
2251
MIZUNO, D.
1784
MIZUTANI, S.
0647, 2368

MKHEIDZE, D.M.
0057, 0144, 0145
MOBARAK, M.A.
1212
MOBBS, B.G.
0448, 0890
MOCHIZUKI, Y.
2495, 2545
MODAN, B.
1175, 1615
MODY, H.
0723
MOERTEL, C.G.
0724
MOHALLATEE, E.A.
2488
MOHIT, B.
1124
MOHR, U.
1345, 1351, 1813,
2242, 2245
MOISE, G.
0983
MOLDOVANU, G.
2132
MOLLO, F.
2113
MOLONEY, J.B.
1472, 1910
MOLONEY, W.C.
0323
MONGA, G.
2113
MONNIER, J.
1375*
MONNOT, P.
0592, 0999
MONROE, J.H.
1023, 1683
MONSON, R.R.
0976
MONTAGNIER, L.
0556, 1079
MONTEMURRO, D.G.
2501
MONTESANO, R.
0086, 0473, 1820
MONTGOMERY, P.O'B., JR.
1825
MONTI, A.
0993
MONTI-BRAGADIN, C.
1517*
MONTIEL, M.M.
0531
MONTREUIL, J.
0495
MOORE, A.L.
1874
MOORE, D.
1878
MOORE, G.H.
0194, 0837, 1167,
1419, 1469, 1926,
1929, 2346
MOORE, E.G.
1945

MOORE, G.E.
0571, 1996
MORA, P.T.
0568, 1091, 2
MORAILLON, A.
1484
MORBIDELLI, R.
2055*
MOREL, C.
1203
MORERA, A.M.
1642
MORGAN, A.
0326
MORGAN, C.
1521
MORGAN, D.G.
0619
MORGAN, D.L.
0931
MORGAN, H.R.
1948
MORGAN, J.F.
2509
MORGAN, L.G.
2043
MORGAN, W.D.
1512
MORGENROTH, K., JR.
1307
MORGENROTH, V.H.,
2064
MORI, H.
1765
MORI, M.
0784, 2381
MORI, Y.
1029, 1030
MORIN, O.
0705
MORISHITA, M.
2381
MORIJA, A.
1560
MORIWAKI, K.
0102, 0716
MOROWITZ, D.A.
1708*
MORRIS, H.P.
0293, 1651,
2050, 2056,
2495, 2498,
2512, 2545,
MORRIS, P.J.
0718
MORRIS, S.
0782
MORRIS, V.L.
1056
MORRISON, S.D.
1703
MORROW, R.H.
1973
MORSE, P.A.
0807
MORSE, P.A., JR.
0643

RTENSEN, E.
 1220
 RTON, D.L.
 0147, 0695, 0704,
 0710, 1536, 1880,
 1984, 1985, 2016
 SCARINI, M.
 2586*
 SGOVICI, C.
 0583, 1891
 SKOVKINA, O.YA.
 1075, 1448, 1477,
 2323
 SLANDER, V.
 1614
 TOMIYA, Y.
 0511
 ULTON, J.E.
 0027
 UNIER-KOHN, P.
 0851
 UNT, B.M.
 0746
 YNE, M.A.
 0819
 CSI, I.
 1045
 ELLER, B.
 0577
 ELLER, D.
 2564
 ELLER, R.
 1010
 ENCH, K.H.
 2510
 LCAHY, M.F.
 2126
 LDAL, S.
 1256
 LHERN, J.E., JR.
 2134
 LICK, S.
 0245
 LLIGAN, R.M.
 1740
 LOCK, B.M.
 1636
 LVIHILL, J.J.
 0012
 MFORD, D.M.
 2343
 NK, K.
 0662
 NN, R.J.
 1874
 NSHOWER, J.
 2498
 NSON, B.R.
 0601, 1032
 NTINGHE, O.G.
 0713
 NYON, W.
 2336
 RAKAMI, N.
 0823
 RAMATSU, E.
 2284

MURANYI-KOVACS, M.I.
 0378*
 MURATA, M.
 0151
 MURPHY, D.L.
 1835
 MURPHY, E.
 0125
 MURPHY, F.A.
 0185
 MURPHY, W.H.
 0310, 1431
 MUSHINSKI, J.F.
 1564
 MUSTACCHI, P.
 0278
 MUTO, T.
 1155
 MYERS, B.
 2410
 MYERS, D.D.
 0562, 0597, 0802
 MYNORS, L.S.
 1180
 NABIZADEH, I.
 2488
 NACHTIGAL, M.
 1100, 1490, 1491,
 1498, 2372
 NADKARNI, J.
 1697
 NADKARNI, J.S.
 1697
 NAEGELE, R.F.
 2301
 NAGAI, H.
 0331
 NAGAKI, D.
 1515
 NAGASAWA, H.
 0312, 0440, 0770,
 0927, 1207
 NAGATA, C.
 0472, 1745
 NAGAYEVA, L.I.
 1473
 NAGAYO, T.
 0040
 NAGEL, G.A.
 2438, 2466*
 NAHAMIAS, A.
 0002
 NAHMIAS, A.J.
 0185, 1061
 NAIB, Z.M.
 0185
 NAIK, S.N.
 2036
 NAIMARK, A.
 0542
 NAITO, M.
 1028, 1029, 1030,
 1063
 NAJARIAN, J.S.
 1582*
 NAKAJIMA, K.
 0666, 1503, 1951

NAKAKUKI, K.
 0172, 0594
 NAKAMURA, T.
 0035, 1354
 NAKAO, K.
 1138
 NAKASHIMA, S.
 1994
 NAKAYAMA, S.
 0797
 NAKAZAWA, I.
 1639, 2058
 NAMBA, M.
 0, 94, 1824
 NANDI, S.
 2345, 2349
 NANKIN, H.
 1710*
 NARAYAN, R.A.
 1305
 NASH, M.A.
 2400*
 NASTAC, E.
 2365
 NATHANSON, L.
 0230, 2567
 NAVARRETTE, A.R.
 2588
 NAYAR, R.
 1292
 NAYAR, K.R.
 0565, 1701
 NAZARIAN, K.
 1465, 1916, 2310
 NEAL, C.
 2258
 NEBERT, L.W.
 0891
 NEGROMI, G.
 1104, 2391
 NEIDHARDT, F.C.
 2506
 NEIMAN, P.E.
 1201
 NEISS, E.S.
 0863*
 NELSON, A.I.
 0519*
 NELSON, R.C.
 1274
 NELSON, R.L.
 1331, 2197
 NELSON-REES, W.A.
 0591
 NERUP, J.
 0773
 NESBIT, M.E.
 1518*
 NETTESHEIM, P.
 2001
 NEUHAUS, O.W.
 1386
 NEUMANN, F.G.
 0031, 0412, 2271*
 NEURATH, A.R.
 0614, 1046
 NEVS, AYA, T.P.
 2574*

NEWBERNE, P.M.
 0915, 2210
 NEWELL, G.R.
 0260, 1617
 NEWMAN, D.
 0542
 NEY, R.L.
 2537
 NEYMAN, I.M.
 2176*
 NEZELOF, C.
 1685
 NG, T.
 1770
 NGAMWATANA, W.
 0967
 NGU, V.A.
 0573
 NIAL, H.D.
 0582, 1027
 NIAS, B.C.
 1607
 NICHOL, F.R.
 1444
 NICHOLLS, E.M.
 2583*
 NICHOLS, W.W.
 0866*
 NICHOLSON, M.O.
 2298
 NICKERSON, N.H.
 0308
 NICOLA, P.
 1760*
 NICOLLE, M.F.D.
 0747*
 NIELSEN, H.R.
 0336*
 NIELSEN, M.H.
 0593
 NIELSEN, S.L.
 1821
 NIEMCZYK, H.
 0137
 NIEPELT, N.
 1762
 NIGRO, N.
 2021*
 NII, S.
 2334
 NIKI, Y.
 0509
 NIKOLOVA, M.E.
 0382*
 NIKULIN, A.
 1850
 NILSSON, A.
 1016*, 1379, 2285
 NIRENBERG, M.
 0783
 NISHIHARA, E.
 0092
 NISHIHARA, H.
 0092
 NISHIKAWA, K.
 0035
 NISHIMURA, E.T.
 0324

NISHIOKA, B.
 1627
 NISHIWAKI, H.
 1560
 NISHIYAMA, H.
 0267, 0271, 0275
 NISHIYAMA, R.H.
 2562
 NISKANEN, E.
 0901, 2070
 NITAVSKAYA, S.D.
 1473
 NIVINSKAYA, M.M.
 0830*
 NOBEL, T.A.
 1411
 NODL, F.
 0778
 NOGALES FERNANDEZ, F.
 0514*, 0742
 NOGUCHI, A.
 0823
 NOGUCHI, S.
 0823
 NOONAN, K.D.
 0679
 NORBERG, R.F.
 0802
 NORBY, K.
 0289
 NORDEN, A.
 2517
 NORDLING, S.
 1002
 NORDQUIST, J.
 1855
 NORMAN, T.
 0828*
 NORONHA, F.
 0163, 0164, 2131
 NORPOTH, K.
 0106
 NORREY, E.
 2397*
 NORREY, K.
 2052
 NORRIS, F.D.
 2133
 NORRIS, H.J.
 0267
 NORTH, J.A.
 1496
 NOSNY, M.A.
 2437
 NOTKINS, A.L.
 0882*
 NOVELL, A.
 0122*
 NOVROGRODSKY, A.
 0236, 1377*
 NOVOTNA, L.
 2429
 NOWAKOWSKI, T.K.
 2576*
 NOWINSKI, R.C.
 0837, 2395*
 NOYES, W.F.
 0200

NYHOLM, K.
 0336*
 NYSTROM, S.
 0303*
 OBARA, T.
 1687
 OBARA, Y.
 0234, 1224
 OBOCHI, S.
 0575
 O'BRIEN, V.L.
 2134
 OBRICAT, F.
 0461
 OBUKH, I.E.
 0654, 2367
 OCHIAI, M.
 2270*
 OCHSNER, A.
 1741
 OCKEN, F.R.
 1321
 O'CONNOR, T.E.
 1954
 O'CONNOR, G.T.
 2341
 ODA, T.
 0094, 1080
 ODAKA, T.
 0169
 ODASHIMA, S.
 0055, 0091,
 ODILI, J.L.
 1131
 O'DONNELL, P.V.
 2395*
 OEHLERT, W.
 0044, 0645
 OETJEN, L.H., JR.
 0825*
 O'GARA, R.W.
 0073
 OGATA, K.
 1575
 OGILVIE, B.
 2118
 OGINO, T.
 2324
 O'HARA, G.P.
 1339
 O'HARA, J.
 1705
 OHBA, Y.
 1905
 OHKUMA, S.
 1784
 OHMORI, S.
 1017
 OHNO, R.
 1560
 OHTA, A.
 1826
 OHTAKI, N.
 1248
 OHYAMA, H.
 2293
 OJALA, A.
 1595

LA, D.
 2528
 DA, H.
 1398, 1399
 JIMA, E.
 0511
 MOTO, T.
 1017
 NO, H.
 2347
 NO, T.
 1355
 ZAKI, E.
 0395
 BO, S.
 1999
 MURA, Y.
 2282
 NEWICK, J.P.
 0307
 NUKI, K.
 0035
 L.J.
 0837, 1427, 1975,
 1977, 2395*
 FFE, J.
 0981
 INIK, G.I.
 0686*
 VER, J.A.
 1505, 1508, 2374
 VI, M.
 0192, 2445
 IN, J.L.
 1894
 ON, C.
 2129
 ON, R.L.
 1855
 SON, H.
 0109
 ENY, C.L.M.
 2493
 RI, Y.
 0093, 0967
 RA, G.A.
 2083
 RA, S.
 1098
 CAL, R.M.
 0261
 ILL, B.J.
 2011
 ILL, F.J.
 2339, 2342
 ILL, R.T.
 1566
 K.
 1028, 1029, 1030,
 1063
 T.
 1138, 2546
 A, K.
 0093
 A, T.
 1029, 1030
 ERA, K.
 0212

OOTA, K.
 1155
 OOTA, S.
 0658
 OPPENHEIM, S.
 0165
 ORAVEC, C.
 2417
 OREN, M.E.
 1520, 1531
 ORIEL, J.D.
 2396*
 ORLOV, A.B.
 0732*
 ORMEROD, M.G.
 0523
 OROSZLAN, S.
 0552, 0562, 2356,
 2407, 2457, 2458
 ORR, D.J.
 0485
 ORTIZ LE LANDAZURI, M.
 0707
 OSHIMA, H.
 0765*
 OSHIRO, K.
 0126
 OSHIRO, L.S.
 1447
 OSIPOV, N.YE.
 2319
 OSSWALD, H.
 0906
 OSTEHMAN, J.V.
 0683
 OSTRETSOVA, I.B.
 1288
 OSTROWSKI, K.
 2420
 OSTRYANINA, A.D.
 2234
 OSUNKOVA, B.O.
 0573
 OTAKI, N.
 2542, 2543
 OTH, J.
 1547
 OTIS, R.D.
 2566
 O'TOOLE, C.
 2015
 OTSU, H.
 1336
 OTTEN, J.A.
 1348
 OTTO, H.D.
 0285
 OXFORD, J.S.
 1055, 2303, 2331
 OXMAN, M.N.
 0209, 2371
 OYASU, R.
 0907
 OZAKI, T.
 0306, 1682
 OZKAN, A.U.
 0987*

OZOHAN, M.L.
 1782
 PACHES, L.R.
 0830*
 PACIFICO, E.
 2193
 PAGANO, J.S.
 1502, 2369
 PAI, S.R.
 2552
 PAINTRAND, M.
 2108
 PALMER, D.L.
 2063
 PALMER, M.S.
 2230
 PALOYAN, D.
 0803
 PALOYAN, E.
 0803
 PAMUKCU, A.M.
 0899
 PANIJEL, J.
 0238
 PANKOJ, E.YA.
 0817
 PAOLETTI, C.
 1270
 PAOLETTI, E.G.
 0089
 PAOLETTI, P.
 0089, 0963, 0964
 PAPAC, R.J.
 0239
 PAPANEK, M.
 1837*
 PAPATHEODOROU, T.
 0106
 PAPOUSEK, F.
 0922
 PAPOYAN, S.A.
 0443
 PAPPAS, A.
 1720*
 PARACHE, R.M.
 1159
 PARAF, A.
 0819
 PARAN, M.
 0779
 PARDO, M.
 1296, 2330
 PARISER, R.J.
 1960
 PARK, S.K.
 1116
 PARKER, A.M.
 0231
 PARKER, J.E.
 0297*, 2480
 PARKHOMENKO, I.I.
 2194
 PARKHOUSE, R.M.E.
 2007, 2008
 PARMENTIER, C.
 1410*
 PARMENTIER, N.
 1410*

PARMI, L.
 0099
 PARMIANI, G.
 1584
 PARNES, V.A.
 0860
 PARODI, S.
 0401
 PARR, I.B.
 1033
 PARROTT, J.C.W.
 1782
 PARSHAD, R.
 1143
 PARSONS, J.
 1911
 PARSONS, J.T.
 0584
 PARSONS, R.L.
 0825*
 PARTURIER-ALBOT, M.
 1592, 1599*
 PASCOE, J.M.
 2248, 2254
 PASQUALINI, C.D.
 1523
 PASS, F.
 2017
 PASTAN, I.
 2315
 PASTERNAK, C.A.
 0256
 PATILLO, R.A.
 0252
 PATOCKA, F.
 1836*
 PATOKIN, S.V.
 2469
 PATRONO, C.
 1690
 PATTERSON, D.S.P.
 0917
 PATTERSON, L.T.
 1915
 PATTILLO, R.A.
 1653
 PAUL, J.S.
 1625
 PAULSCH, W.E.
 0690*
 PAULUZZI, S.
 1456, 2326
 PAVLOVSKY, A.
 2136
 PAYAN, H.M.
 0722
 PAYMASTER, J.C.
 1419, 2487
 PAYNE, F.E.
 0262
 PAYNE, L.N.
 0162
 PAYNE, R.E.
 2375
 PEARCE, M.L.
 1363
 PEARSE, A.G.E.
 0740

PEARSON, F.G.
 2203
 PEARSON, J.W.
 0196
 PEARSON, G.H.
 2226
 PEASE, P.
 1726
 PECKHAM, M.J.
 1236
 PEDIC, G.
 2143*
 PEDLEY, S.F.
 0115
 PEGG, A.E.
 2216
 PEGRUM, G.D.
 0714
 PEILLON, F.
 2580*
 PEKAREK, J.
 1538
 PELLAR, J.
 2576*
 PELLER, P.
 0152
 PELLETIER, G.
 2580*
 PEMBERTON, M.
 1696
 PENMAN, H.G.
 0505
 PENN, G.M.
 1127
 PENN, I.
 0839, 2138
 PENNELLI, N.
 1970
 PENNEYS, N.S.
 0134
 PEPPERS, E.V.
 1143
 PERCY, D.H.
 1461, 2502
 PERDOMO, J.T.
 0048
 PERIMAN, P.
 1546
 PERIN, F.
 0411
 PERIN-ROUSSEL, O.
 0411
 PERK, K.
 1411, 1930
 PERLMUTTER, A.
 2522
 PERMAN, V.
 1877
 PEROCCHO, P.
 1989
 PERRY, S.
 2170*
 PERSSON, B.
 0526
 PERTAYA, A.V.
 1526
 PESKOVA, V.I.
 1596

PESTIAU, J.
 0187
 PETERKOFISKY, A.
 2518
 PETERS, J.H.
 1758*
 PETERS, R.F.
 1394
 PETERS, R.L.
 0562, 0602, 17
 PETERSON, A.R.
 2291
 PETO, R.
 1798
 PETRAKIS, N.L.
 2094
 PETROVA, A.S.
 0327
 PETROW, Z.D.
 0379*
 PETRUN, A.S.
 1318
 PETSKA, S.
 0790
 PETTERSSON, U.
 0613, 1043, 19
 PEYDRO, A.
 1373*
 PEYDRO OLAYA, A.
 1785
 PFITZER, P.
 0736
 PHAN, H.H.
 2214
 PHAN HUN TRUNG, M.
 2580*
 PHEMISTER, R.D.
 0525
 PHILIP, P.
 0030, 1146
 PHILIPSON, L.
 0613, 1912
 PHILLIPS, A.J.
 0767*
 PHILLIPS, B.
 1306
 PHILLIPS, F.S.
 0058, 2218, 2
 PHILLIPS, P.A.
 2316
 PHILLIPS, R.W.
 0788
 FICK, C.R.
 2476
 PICKLEMAN, J.R.
 0803
 PICKRELL, J.A.
 1013, 1014, 1
 PIENTA, R.J.
 1969
 PIERCE, G.B.
 1588
 PIERRE, R.V.
 0507, 1147
 PIESSENS, W.F.
 0840, 1243, 2
 PIETERSZ, R.N.I.
 0713

KE, G.Z.
 1114
 KULA, B.
 1250
 LCH, D.J.F.
 1450
 LCH, Y.H.
 0077, 0222, 0428,
 1125, 1561, 1988,
 2459, 2464*
 LLINGER, D.J.
 0319, 2088, 2474
 NCUS, R.A.
 0138*
 NCUS, T.
 0606
 NDBORG, J.J.
 0247
 NKHAS, J.
 1643
 NTADO, T.
 0554
 PEK, W.N.
 0671
 RAS, A.
 1456
 RRO, G.
 2025, 2585*
 STER, L.
 0711, 1909
 TOT, H.C.
 0051, 0052, 2549
 TTS, J.D.
 1440
 TZURRA, M.
 0677
 AGEMANN, P.G.W.
 2544, 2572
 AINFOSSE, B.
 1371
 AMENAC, P.
 1850
 ANT, J.E.
 2248
 ANTEROSE, D.H.
 1450
 ATA, E.J.
 0163
 ENERT, L.
 0712, 1738
 ESCIA, O.J.
 0356
 ESKA, O.J.
 2403
 ISS, G.B.
 0023, 0487
 OEM, J.E.
 0713
 UOT, M.
 0127, 0486
 DZEY, L.K.
 1314
 EL, W.E.
 0561
 IRIER, J.
 1402*
 IRIER, L.A.
 0051, 0052

POISSANT, G.
 2562
 POKORNY, J.
 0220
 POLAK, J.
 0799
 POLLACK, R.
 0558, 1507
 POLLIACK, A.
 0449, 0451, 0452
 POLLOCK, R.J., JR.
 2128
 POLONSKI, R.
 1664
 POLYZONIS, M.B.
 1669
 POMPLUN, S.
 1406*
 PONG, R.S.
 0428, 1744
 PONOMAR'KOV, V.I.
 2107, 2319
 PONSSTINGL, H.
 1581*
 PONTEN, J.
 1082
 PONZONE, A.
 1760*
 POOLE, A.R.
 0250
 POPE, J.H.
 0795
 POPE, L.S.
 0780
 POPESCU, N.C.
 2236
 PORIES, W.J.
 1232
 PORTEOUS, I.B.
 0774
 PORTER, I.H.
 2098
 PORTERFIELD, J.S.
 1428
 PORTUGAL, F.H.
 2505
 PORWIT-BOBR, Z.
 1510
 POSKANZER, D.C.
 1831
 POSSEHL, E.A.
 2082
 POST, J.E.
 2131, 2312
 POSTE, G.
 1019
 POTDAR, G.G.
 0752
 POTMESIL, M.
 1842
 POTOLSKY, A.I.
 1123
 POTOP, I.
 0842
 POTTER, A.M.
 2331
 POTTER, C.W.
 1055, 2303, 2331

POTTER, M.
 1736
 POTTER, V.R.
 2549
 POTVIN, R.
 1631*
 POULSEN, H.
 2102
 POUND, A.W.
 0545
 POWELL, L.C., JR.
 1832
 POWLES, R.L.
 2406
 PRADE, M.
 1328
 PRAGE, L.
 0613
 PRAHL, J.W.
 2443
 PRASAD, K.N.
 0567
 PRATESI, G.
 1128
 PRECHTEL, K.
 0152
 PREHN, R.T.
 0942, 1584
 PRESSMAN, D.
 2415
 PRETO, G.
 1719*
 PREUSSMANN, R.
 0032, 0478, 0483,
 0905, 1762, 2252
 PRICE, F.A.
 0063
 PRICE, J.W.
 0036, 0699
 PRIGIONE, L.
 1184
 PRINZ, L.M.
 1239
 PRIS, J.
 1375*
 PRITZKER, K.P.F.
 1118
 PROBATOVA, N.A.
 0327
 PROBST, H.
 2579*
 PRODI, G.
 1362, 1989
 PROFFITT, S.O.
 0131
 PROLLA, J.C.
 0528
 PROPI, S.
 0130
 PRUCHNICK, W.F.
 1522
 PRUNIERAS, R.
 1516*
 PRUSKA-KOEPPE, H.
 0267
 PRUTKIN, L.
 1321

PTAK, W.
1510
PUGH, T.E.
1115*
PUJOL MOIX, N.
0748*
PULLINGER, I.D.
0194
PURCHASE, H.G.
0161, 1467
PURCHASE, I.F.H.
0402, 2135
PUSZTAL, K.
0178, 1045
PUVION, F.
0494, 0495
PYLEVA, Z.A.
0025
QUAN, F.C.
2214
QUETIER, F.
0263*, 1254
QUIJANO, F.
1585
QUINN, C.E.
1200
QUINTRELL, N.
0203, 0645, 0646,
0648, 1081, 1088
RABASA, S.L.
1523, 1557, 2136
RABES, H.
0957, 1350, 1812
RABIN, H.
0650, 1919
RABINOVIC, JE.A.
1634*
RABINOWITZ, Z.
0951
RABOTTI, G.F.
1484, 1527
RABSON, A.S.
2306, 2341
RABSTEIN, L.S.
0167, 0173, 1443
RABUKHIN, A.YE.
2472
RACADOT, J.
2580*
RADNOT, M.
1670
RADOMSKI, J.
0421
RAHN, I.
1851
RAIKHLIN, N.T.
0258, 0259
RAITCHEFF, I.
0815
RAITSCHER, R.
0118*
RAJ, H.G.
0920, 1311
RAJAWAT, D.
1706
RAKHMANNIN, P.P.
2048

RAKIETEN, N.
2186
RALPH, D.D.
1085
RAMALINGASWAMI, V.
0426
RAMMING, K.P.
0077, 0222, 1125,
1561, 1988, 2464*
KAN, M.
1133
RANADIVE, K.J.
1072, 1120, 2081,
2552
RANDELIA, H.P.
2036
RANDERATH, K.
2527
RANDS, E.
1037
RANNIE, I.
2180, 2182
RAO, P.R.
1967
RAPOPORT, A.H.
0808
RAPOPORT, I.A.
0860
RAPP, F.
0213, 0615, 1463,
1982, 2339, 2342,
2565
RAPP, H.J.
0727, 1555, 1992,
2440
RAPP, W.
1580*
RAPPAPORT, H.
0756, 1148
RASKA, K., JR.
1047, 2329
RASKAS, H.
1911
RASKOVA, J.
2403
RATCLIFFE, N.A.
1668
RATH, F.W.
0253
RAUSCHKOLB, E.W.
0918, 1856
RAUSHENBAKH, M.O.
2317
RAVHIAR, B.
1187
RAVICH, A.
2394*
RAVICH, R.B.M.
1206
RAWCLIFFE, R.M.
1858
RAWLS, W.E.
0624, 1924
RAY, R.K.
0143
RAYKHLIN, N.T.
2030

RAYNAUD, A.
2127
RAYNAUD, J.
2127
REAGAN, J.W.
1249
REDDI, A.H.
0738
REDDI, K.K.
2362
REDDY, J.
0024, 2114
REDMAN, H.C.
1014, 1015
REDMAN, L.W.
1770
REDMOND, C.K.
1620
REECE, W.C.
0403
REES, E.O.
0061, 1340
REESE, A.B.
1666
REESE, H.W., JR.
1761
REGNIER, M.
1516*
REICHEL, W.
1581*
REID, E.
1636
REIF, A.E.
1553, 2414, 2
REIF, J.S.
1183
REILLY, C.A.
2322
REINER, J.
0079
REINHARD, J.F.
0119*
REINHARD, M.
1227
REIS, H.E.
0226
REISS, J.
1376*
RENAWEK, K.
1342
RENE, A.A.
0546
RENNIE, M.
0162
RENZETTI, A.D., J.
2261
RESNITZKY, P.
0779
RETH, S.
0220
REUBER, M.D.
0034, 0944,
2549
REUSS, W.
1818
REUSSER, F.
1444

UTER, A.M.
 2497
 VAZOVA, YE.S.
 0595, 2319
 VOL, L.
 0121*
 XED, B.
 1007
 Y, R.K.
 0634
 YNOLDS, R.D.
 2549
 YNOLDS, T.B.
 1712*
 EE, S.U.
 1174
 IM, J.S.
 1326, 2376
 BACCHI, R.
 0637, 0811, 2326
 CCI, N.
 1719*
 CE, J.M.
 2263
 CH, M.A.
 1907, 2313, 2412,
 2456
 CHARD, M.H.
 1949
 CHARDS, A.H.
 2222
 CHARDS, J.F.
 1770
 CHARDSON, L.S.
 1525
 CHART, R.M.
 1157
 CHMOND, I.S.
 2124
 CHTER, G.W.
 2550
 CHTER, M.C.
 1232
 CHTER, W.R.
 0497
 CHTERS, A.
 2079
 CHTERS, V.
 2079
 CKARD, C.G.
 0588, 1976, 2131,
 2312
 CKARD, V.D.
 1623
 DDICK, D.H.
 0791, 2091
 DDLE, P.
 1959
 ECHERS, L.A.
 1322
 EDER, S.V.
 0246
 FKIND, D.
 2063
 GAS, D.A.
 1570
 GBY, C.C.
 2099

RIGBY, P.G.
 0702, 1556
 RIGDON, R.H.
 2258
 RIGGS, V.
 1563
 RILEY, F.C.
 1149
 RIMAN, J.
 0586
 RIMDUSIT, S.
 1706
 RIMOIN, D.L.
 1687
 RIMONDI, C.
 0341*
 RINGERTZ, N.
 0753
 RIOU, G.
 1270, 2308
 RITUCCI, A.
 1404*
 RIXON, R.H.
 0818
 RIZZO, A.J.
 2262
 RJOSK, H.K.
 2271*
 ROBBINS, J.
 0255
 ROBBINS, P.W.
 1514, 2477
 ROBERT, P.K.
 1163*
 ROBERTS, B.A.
 0917
 ROBERTS, G.H.
 1004
 ROBERTS, J.D.B.
 0488
 ROBERTS, J.J.
 2248, 2254
 ROBINSON, D.J.
 1462
 ROBINSON, H.
 2037
 ROBINSON, H.L.
 1085, 1482, 1944
 ROBINSON, W.S.
 1085, 1482, 1944,
 2398*
 ROBINSTON, H.L.
 2398*
 ROCA, A.N.
 0535
 ROCCHI, P.
 1362
 ROCKWELL, M.A.
 1707*
 ROE, F.J.C.
 0065, 1798
 ROGERS, A.E.
 0915, 2210
 ROHRBACH, R.
 1343
 ROIZMAN, B.
 0002, 0621, 1058,
 1062, 2310

ROKUTANDA, H.
 0143, 0634, 2355
 ROKUTANDA, M.
 0143, 0634, 2355
 ROLLAG, M.D.
 1394
 ROM, W.
 1160, 2027
 ROMAGOSA PUIG, V.
 0748*
 ROMANENKO, A.M.
 2028
 ROMANOV, V.I.
 0886
 RONDIA, D.
 0459
 RONGEY, R.W.
 2298
 ROOS, U.
 1137
 ROSAI, J.
 2165*
 ROSCHLAU, G.
 2185
 ROSEMAN, S.
 1958
 ROSEN, S.W.
 1656
 ROSENBERG, R.
 0783
 ROSENGREN, A.M.
 1222
 ROSENGREN, B.
 0526
 ROSENGER, V.M.
 1548
 ROSNER, F.
 0363
 ROSS, E.
 0324
 ROSS, J.
 2320
 ROSSI, G.E.
 0603, 1898
 RUSS-MANSELL, P.
 1315
 ROSVOLL, R.V.
 1173
 ROTERMUND, H.M.
 0305
 ROTH, L.
 0983
 ROTHMAN, I.K.
 1901
 ROTHSCHILD, H.
 0660, 0667
 ROUJEAU, J.
 0371
 ROUNDS, D.E.
 1562
 ROUSE, H.
 0184
 ROUSSEAU, M.F.
 1665
 ROUZEL, P.
 0819
 ROWE, J.M.
 1395

ROWE, N.H.
 0308
 ROWE, W.P.
 0638, 1052, 1115*
 1980, 2332, 2371
 ROWLANDS, D.T., JR.
 1123
 ROWLEY, M.
 1119
 ROWSON, K.E.K.
 0610, 1033
 ROYSTON, I.
 0186, 0623
 ROZENBLATT, S.
 1499
 ROZHKOVA, L.G.
 0515*
 RUBENCHIK, B.L.
 0897
 RUBENCHUK, B.L.
 1318
 RUBIN, A.D.
 0391*
 RUBIN, B.A.
 0614, 1046
 RUBIN, H.
 0644
 RUCKER, U.
 0082
 RUDALI, G.
 2127, 2171*
 RUDALI, M.G.
 0378*
 RUDOLPH, M.
 0672
 RUDOLPH, R.
 1616
 RUECKERT, F.
 0508
 RUECKERT, U.
 0741
 RUETTNER, J.R.
 2143*
 RUHENSTROTH-BAUER, G.
 1387
 RUMPLER, B.
 1343
 RUNGE, W.
 1702
 RUOSLAHTI, E.
 2002
 RUSH, M.G.
 1492
 RUSSELL, D.H.
 0315, 2074
 RUSSELL, E.
 2351
 RUSSELL, W.C.
 2328
 RUSSELL, W.J.
 1854
 RUSSFELD, A.B.
 1259
 RUSSO, A.
 1404*
 RWOMUSHANA, J.W.
 0451

RYAN, W.L.
 0702
 RYDEL, R.E.
 2183
 RYTOMAA, T.
 0901, 2070
 SAAL, F.
 1523, 2136
 SACCOMANNO, G.
 1859
 SACHS, L.
 0661, 0708, 0779,
 0951
 SACKSTEDER, M.R.
 2366
 SACQUET, E.
 0494
 SAEGESSER, F.
 0360
 SAENGER, F.
 0959
 SAEZ, J.M.
 1642
 SAGEBIEL, R.W.
 1687
 SAGEMAN, R.H.
 0124
 SAHEBUJAMI, H.
 1718*
 SAHEKI, K.
 2086
 SAHNAZAROV, N.
 1490, 1491, 1498
 SAID, S.M.
 0771
 SAIDI, F.
 2041
 SAINT CYR, C.DE V.
 2437
 SAIRENJI, T.
 1020
 SAITO, H.
 0170, 1533
 SAITO, M.
 1515
 SAITO, T.
 1359, 2359
 SAKAI, T.
 1803
 SAKAUE, Y.
 2393*
 SAKNYN, A.V.
 1185
 SAKSELA, E.
 0303*, 0530, 0875*,
 1002
 SAKURAI, M.
 0800
 SALABE, G.B.
 0255
 SALAK, D.
 2050, 2499
 SALAMAN, M.H.
 0610
 SALAS, J.
 1507
 SALBER, E.J.
 1187

SALIER, B.
 0520*
 SALIMI, R.
 0254
 SALVAGGIO, J.
 0103
 SALZANO, F.M.
 1680
 SALZMAN, L.A.
 1071, 2300, 23
 SAMPSON, C.C.
 1623
 SAMUELS, L.T.
 0022
 SAN, R.H.C.
 0968, 1356
 SANBE, M.
 1414
 SANCES, A., JR.
 0252
 SANCHIS-BAYARRI LAH
 0730*
 SANCHIS-BAYARRI VAI
 0730*
 SANDBERG, A.A.
 1235, 1252, 17
 2175*
 SANDER, J.
 1819, 2184
 SANDER, S.
 0064, 0828*
 SANDERS, C.L.
 1843
 SANDERS, F.K.
 2395*
 SANDOR, T.
 2032*
 SANDRITTER, W.
 1640, 1775
 SANEYOSHI, M.
 1357
 SANFORD, B.H.
 1552
 SANFORD, K.K.
 1143
 SANO, M.
 2067
 SANPE, T.
 0151
 SANS-SABRAFEN, J.
 0748*
 SANTESSON, B.
 0521
 SANTESSON, L.
 0574
 SANTI, L.
 0122*
 SANTIAGO, M.
 0517*
 SAPIRA, J.
 1710*
 SAPRIN, A.N.
 1048
 SARDESAI, S.
 2460
 SARGENTINI, S.
 1690

RKAR, N.H.
 0837, 1419, 1469
 RMA, P.S.
 0562, 0582, 1871,
 1888, 1977, 2311,
 2413
 RRAZIN, G.
 1771
 SAKI, M.
 1224, 1691
 SAKI, M.S.
 1008
 SAKI, T.
 0309
 TO, C.
 1136
 TO, H.
 0098, 0490, 0958
 TO, J.
 1824
 TO, K.
 1359, 2086
 TO, S.
 1658
 TO, T.
 1983
 TPAYEVA, R.A.
 0760
 UER, G.
 0214, 2377
 UER, R.
 0582, 1027
 UNLERS, R.P.
 1859
 VAGE, T.
 0621
 VEL, H.
 0645
 VLUCHINSKAYA, L.A.
 2239
 WICKI, W.
 1931
 XEN, E.
 0303*, 2117
 YED, B.A.
 2038
 AIFE, J.F.
 0614
 CAMPS, R.A.
 2011
 CANLON, M.D.
 2400*
 CANO, A.
 0803
 CEVOLA, M.E.
 1506
 CHACHT, U.
 1352
 CHAEFER, C.
 2473
 CHAEFER, P.K.
 0765*
 CHAEFER, Y.
 0045, 0711, 1909,
 2312
 CHAEFFER, B.T.
 2206

SCHAFFER, P.
 1060
 SCHAGEN, B.
 0090
 SCHALLER, A.
 1261
 SCHARFF, M.D.
 2005, 2421
 SCHAUDIG, G.
 2573*
 SCHAUER, A.
 2024
 SCHAUF, V.
 1936
 SCHEIN, P.S.
 2186
 SCHELLANDER, F.
 1368
 SCHEPERS, G.W.H.
 1748, 1749, 1750
 SCHER, C.D.
 2370
 SCHER, W.
 1897
 SCHERF, H.R.
 0904, 1815
 SCHERMULY, W.
 2473
 SCHERRER, K.
 1203
 SCHERRER, R.
 0819
 SCHERSTEN, T.
 1645
 SCHEURLIN, P.G.
 1720*
 SCHIDLOVSKY, G.
 1965, 1985
 SCHIEFER, H.G.
 2163
 SCHIFFER, A.
 1276
 SCHIFFER, D.
 0089, 0963, 0964
 SCHILLER, A.L.
 1821
 SCHILLING, G.
 1805
 SCHLABACH, A.
 2561
 SCHLAUDER, M.C.
 2195
 SCHLEDE, E.
 0939, 1334, 1335
 SCHLESINGER, R.W.
 0184
 SCHLOM, J.
 0141, 0142, 0553,
 1472, 1878, 1910
 SCHLOSS, G.T.
 1451, 2322
 SCHLOTE, W.
 1227
 SCHLUMBERGER, J.R.
 2108
 SCHMAEHL, D.
 0435, 0906, 1815

SCHMAHL, D.
 1351
 SCHMALZI, F.
 2584*
 SCHMICKEL, R.D.
 2375
 SCHMID, W.
 0903
 SCHMIDKE, H.H.
 1821
 SCHMIDT, A.
 2244
 SCHMIDT, F.
 0880*
 SCHMIDT, F.W.
 0711
 SCHMIDT, N.F.
 1644
 SCHMIDT-BAUMLER, U.
 0988*
 SCHMITTER, R.
 1023
 SCHNAITMAN, C.A.
 1652
 SCHNECK, S.A.
 2136
 SCHNEIDER, R.
 0277, 2039, 2288
 SCHNEIDER, W.C.
 1660
 SCHNYDER, U.W.
 2026
 SCHOENBERG, B.S.
 1181
 SCHOENTAL, R.
 0033, 2256
 SCHOLEFIELD, P.G.
 2539
 SCHOLLE, R.H.
 0396
 SCHOLZE, P.
 0957, 1350
 SCHON, E.
 0229
 SCHORR, I.
 2537
 SCHOTTENFELD, D.
 0011, 1621
 SCHRAMM, G.
 0692
 SCHRAMM, T.
 0672, 1285, 1451,
 1956, 2187
 SCHREIBER, D.
 0965
 SCHREIBER, G.
 0305
 SCHREMMER, C.N.
 1672, 2238
 SCHROEDER, E.C.
 0048
 SCHROEDER, T.M.
 0856
 SCHULER, D.
 0330
 SCHULLER, P.L.
 0990*

SCHULSON, N.G.
1857
SCHULT-HOLTHAUSEN, H.
0574
SCHULTZ, A.M.
1956
SCHULTZ, D.R.
1698
SCHULTZ, G.
1766
SCHULTZ, M.D.
0132
SCHULTZ, W.D.
2272*
SCHUMANN, J.
1722*
SCHWABITZ, G.
0112
SCHWARTZ, F.D.
2366
SCHWARTZ, R.S.
0224, 0230
SCHWARZ, J.
1581*
SCHWARZ, L.H.
0884
SCHWARZMAIN, W.
1760
SCHWELBACH, G.
1496
SCHWEISGUTH, O.
1371
SCOLNICK, E.M.
0557, 0589, 1037,
2320
SCORRETTI, L.
1153
SCOTT, C.D.
0503
SCOTT, G.
0321
SCRIBNER, J.
0408
SEARLE, J.H.A.
0269
SEEBERGER, K.E.
0334*
SEEL, D.J.
1174
SEEMAYER, N.
1537
SEGALOFF, A.
1295
SEGEV, Y.
2402
SEIBERT, F.B.
2124
SEIDEL, E.H.
1693, 1885
SEIDLOVA, A.
2538
SEIDLOVA, B.
2465*
SEIDMAN, H.
0296*
SEIFERT, E.
0711

SEIGLER, H.F.
1542
SEIJI, M.
2542, 2543
SELA, B.A.
0708
SELIRIO, E.S.
0150
SELKIRK, J.K.
1651, 2221
SELLYEI, M.
2273*
SEMENOVA, L.A.
1038
SENDA, H.
2084
SENDU, F.
0170, 1533
SENIK, A.
0165
SENTURIA, B.H., JR.
0042
SENYSYN, J.J.
0133
SEPPAELAE, M.
2002
SERBAN, V.
0983
SERGEYEV, A.V.
2317
SEPINGE, P.
1371
SERONDE, J., JR.
0311
SERRA, A.
1690
SERY, T.W.
1234
SETH, R.K.
1624
SEVER, J.L.
1061
SEYDEWITZ, V.
0139*
SEYMOUR, R.J.
1832
SHABAD, L.M.
2228, 2239
SHABYNINA, N.K.
1185
SHALKOP, W.T.
1778
SHANI, M.
1175
SHANK, R.C.
1777
SHANKARAN, R.
0920, 1311
SHANMUGARATNAM, K.
1165
SHARMA, O.K.
2511
SHARON, N.
0708
SHARON, Z.
1175
SHARPE, C.A.B.
2093

SHATALOVA, G.G.
103P
SHAW, M.W.
2174*
SHCHERBAKOVA, O.E.
1042
SHEARER, R.W.
2212
SHEBA, C.
1175
SHEDO, D.P.
1612
SHEID, B.
2512
SHEININ, R.
0212, 0218, 110
1110
SHELLABARGER, C.J.
1847
SHER, A.
2444
SHERBET, G.V.
0293, 0392*
SHERIDAN, B.
0321
SHERR, C.J.
2009
SHERPILL, M.N.
1005
SHERWIN, R.P.
2079
SHETH, N.A.
2081
SHEVELEV, B.I.
1448
SHEVLIAGHYN, V.J.
0207, 0675
SHEVLYAGIN, V.Y.
0655
SHEYKI, P.I.
1594
SHIBUYA, C.
0895
SHIDA, K.
0331
SHIDOO, T.
1219
SHIHABI, Z.
1386
SHIMAZAKI, J.
0331
SHIMIZU, T.
1437
SHIMKIN, N.B.
1327, 1792
SHIMOO, J.
1458, 1978
SHIMOSATO, Y.
0322
SHIPOVA, L.JA.
2003
SHIRAI, T.
1034, 1533
SHUKASHVILLI, N.N.
0793
SHIVELY, J.N.
0525

KLAR, G.
1541, 1788
LYANKEVICH, M.A.
0207
OPE, R.E.
1995
OPE, R.E., JR.
1877
ORTTRIDGE, K.F.
0183
UBIK, P.
0513*, 1330
UBIN, A.S.
0259, 2107
UBLAUZE, A.K.
1418
UCK, A.
0061
UGART, L.R.
2521
BAL, L.R.
0163, 2409
CILIANO, M.J.
2522
EGLER, R.
1729
GEL, M.M.
2436
GLER, P.B.
1913
BER, R.
1901
LVERBERG, E.
0279, 1602
LVERBERG, H.
1435
LVERSTONE, H.
0269
MAGA, D.
1266*
MARD, R.
0368
MKOVIC, D.
1488
MMONS, R.L.
1582*
MS, E.S.
2006
MPSON, E.
2118
MPSON, J.S.
2060
MPSON, W.L.
0060
MS, P.
0066, 0067
NCLAIR, W.K.
0129, 2290
NGER, H.
1692
IGH, D.V.
0769
NKOVICS, J.G.
1969, 2558
NKS, L.F.
0694
NN, I.
0537

SINNHJBER, R.O.
1308
SIRACKA, E.
0810
SIRACKY, J.
0810
SIRSAT, S.M.
1419
SIVAK, A.
2204
SJOGREN, H.O.
0180, 0656, 2455
SJOLIN, K.E.
0336*
SKATKOV, M.E.
0886
SKIBBA, J.L.
0423
SKINNER, M.
0230
SKINNER, M.S.
2340
SKIPSKI, V.P.
0785, 2068
SKOGLUND, R.W.
1161
SKREB, N.
0317, 1671
SLABBER, C.F.
0248
SLADE, T.A.
0933
SLATTERY, S.M.
1965
SLESERS, A.
2495, 2545
SLIFKIN, M.
1296, 2330
SLOW, I.N.
1408*
SMALL, E.
1151
SMART, C.R.
1614
SMIDA, J.
2363
SMIDOVA, V.
2363
SMIECINSKI, W.
2235
SMIRNOV, G.A.
2228
SMIT, C.G.S.
0506
SMITH, B.A.
2254
SMITH, C.A.
0642
SMITH, C.E.
2198
SMITH, D.F.
0429
SMITH, G.H.
0631, 1422, 1927
SMITH, H.
1668
SMITH, H.H.
0539

SMITH, H.S.
2370
SMITH, J.A.
0338*, 0834
SMITH, J.B.
1566
SMITH, J.D.
0918
SMITH, J.K.
1776
SMITH, J.L.
2083
SMITH, J.L., JR.
0535
SMITH, J.W.
0176
SMITH, L.H.
0533
SMITH, M.
2568
SMITH, M.N.
2565
SMITH, P.D.
2561*
SMITH, R.A.
1210
SMITH, R.T.
2435
SMITHERS, D.W.
1218
SMOLEN, V.F.
0075
SMOLER, D.F.
1446
SMOLER, J.
1168
SMUCKLER, E.A.
1783
SMULLYAN, I.
2188
SMYK, B.
1270
SHAJD, V.
0227
SNIDER, M.E.
1460
SNODGRASS, M.J.
0174, 0609, 2001
SNYDER, D.E.
0075
SNYDER, S.H.
0315
SNYDER, S.P.
1872
SO, B.T.
2241
SOCQUET, M.
1223
SOEHNER, R.L.
1938
SOGA, J.
1590
SCHIER, R.
0757
SOKOLOV, P.P.
0144
SOKOLOVA, E.V.
0455

SOLOFF, B.L.
 1663
 SOLTER, D.
 0317, 1671
 SOMEDA, K.
 1991
 SOMOGYI, A.
 0438, 2217, 2227
 SONLEY, M.J.
 1578
 SONTAG, J.M.
 2276, 2278
 SOO, S.F.
 1552
 SOOFI, G.S.
 1894
 SOREN, L.
 0697
 SORENSEN, D.K.
 1877
 SOROF, S.
 0050, 1317
 SOROKINA, Y.D.
 0477, 2231
 SOSKIND, L.
 0884
 SOSNIK, H.
 2190
 SOULE, H.D.
 0166
 SOULEIL, C.
 0238
 SOURANDER, P.
 1007
 SOUTHAM, C.M.
 1140
 SPAHN, G.
 1933
 SPAHN, G.J.
 0602
 SPAIN, J.D.
 2213
 SPEAR, P.G.
 0002, 0621, 1062,
 2310
 SPECTOR, E.
 0119*
 SPEICHER, C.E.
 1518*
 SPEIZER, F.E.
 2043
 SPEZIA, C.A.
 0502
 SPIEGELMAN, S.
 0141, 0142, 0553,
 1878, 2299
 SPIESS, H.
 1000
 SPJUT, H.J.
 0744, 2565
 SPOHR, G.
 1203
 SPOONER, T.R.
 0131
 SPORN, M.B.
 2179
 SPRECHER-GOLDBERGER, S.
 0187

SPRENGER, E.
 1640
 SPRIGGS, A.I.
 2467
 SPRINGER, J.
 0044
 SPRINGER, P.
 0044
 SPRYSKOVA, M.A.
 2220
 SQUARTINI, F.
 0192, 0628, 0632,
 2286, 2344
 SQUIRE, R.
 0301*
 SQUIRES, C.
 2148
 SRINIVASAN, D.
 2090
 SRINIVASAN, P.R.
 2090
 SRIVANNABOON, S.
 2014
 SRIVATANAKUL, P.
 1981
 STAHLER, F.
 0537
 STAEMMLER, M.
 0564
 STANCIU, G.
 0140*
 STANCFAST, S.J.
 2042
 STANFORD, G.B.
 1666
 STANISLAWSKI, M.
 0819
 STANKEVICH, M.P.
 0763
 STANLEY, N.F.
 2316
 STARA, J.
 1274
 STARK, O.
 0706, 0900
 STASEK, V.
 0768*
 STASINOPOULOS, M.
 0374
 STAUGAARD-KLOOSTERZIEL,
 2556
 STAVRAKY, K.M.
 0318, 2264
 STAVROUS, D.
 0966
 STEERS, A.K.
 1140
 STEEVES, R.A.
 1900, 1902
 STEFANI, S.
 0693
 STEFANOVIC, J.
 2274
 STEGGLES, A.W.
 0834
 STEINBACH, K.H.
 1405*

STEINBERG, M.P.
 0519*
 STEILER, T.
 0228
 STEINGLASS, M.
 1202
 STEINHOFF, D.
 1767
 STELLWAGEN, R.H.
 2078
 STENBACK, F.
 1323, 1595
 STENBACK, W.A.
 1417, 1868, 23
 STENGLEIN, B.
 1879
 STENHOUSE, W.S.
 2049
 STENMAN, S.
 1002
 STEPHENS, D.
 0780
 STEPHENS, K.
 2431
 STEPHENS, R.
 0175
 STERN, D.
 1408*
 STERN, E.
 0120*, 0281
 STERN, K.
 2405
 STERNBERG, S.S.
 2218
 STEVENS, D.
 0154
 STEVENS, D.A.
 1466, 1578
 STEVENS, D.F.
 1563
 STEVENS, L.C.
 0304
 STEWART, A.
 1605
 STEWART, A.M.
 0690*
 STICH, H.F.
 0968, 1356
 STICKL, H.
 1879
 STILL, W.J.S.
 2105
 STILLE, W.T.
 0115
 STILLER, D.
 0085
 STILLMAN, A.
 0362
 STILMANT, M.M.
 2438
 STITT, D.
 1021
 STJERNSWAERD, J.
 2015, 2418
 STOBBE, H.
 0379*
 STOCK, C.C.
 0785, 2068

STOCK, J.A.
1680
STOCK, N.D.
1873, 1876
STOCKS, P.
0280, 2047
STOFFYN, P.
2563
STOIAN, M.
2365
STOKER, M.
0350, 2390
STOKER, M.G.P.
0216, 1959
STOLOFF, I.L.
1221
STOLS, A.L.H.
0607
STOLZMANN, W.M.
1678
STONE, H.A.
0160
STONE, L.B.
1096, 2297
STONE, N.H.
0531
STONE, R.A.
0503
STONEHILL, E.H.
0721
STOPCHANSKAYA, A.G.
0686*
STOUGHTON, R.B.
0536
STRAIN, W.H.
1232
STRANDBERG, B.
1912
STRAUCH, L.
1649
STRAUS, F.H.
0803
STREETER, A.M.
2011
STREETT, C.S.
0301*
STRICKER, M.
1601*
STRICKLAND, P.
1849
STRIMLAN, C.V.
1522
STROHL, W.A.
0184, 1047, 2329
STRUM, S.B.
0756, 1148
STRYCKMANS, P.
1223, 1732, 2563
STUART, A.
1250
STUART, J.
2060
STUBBS, K.G.
1460
STULBERG, C.S.
1126
STULBERG, M.P.
2521

STUMPHIUS, J.
2046
STURROCK, J.E.
2248
SUBBUSWAMY, S.G.
2066
SUDAREV, P.V.
2161
SUEMASU, K.
0322
SUERE, J.T.
0975
SUESS, M.J.
0865*
SUESS, R.
0408, 0447, 0892
SUGANO, H.
1937
SUGAR, J.
1152
SUGIHARA, R.
0430
SUGIMOTO, A.
1217
SUGIMOTO, T.
0431, 2211
SUGIMURA, T.
2253
SUGIYAMA, H.
0709
SUKOVATYKH, L.S.
0763
SULITZEANU, A.
2402
SULITZEANU, S.
2447
SULLIVAN, D.
0646, 1088
SULLIVAN, P.D.
1611
SUMIE, H.
0907
SUN, S.C.
2206
SUNDERMAN, F.W., JR.
2154
SUNDER-PLASSMANN, M.
1262
SUNE, M.V.
1689
SURJAN, M.
0843
SUROWIAK, J.
2287
SJSANIA, L.
1622
SUTHERLAND, R.M.
1675, 1998
SUTOW, W.W.
0529
SUZUKI, E.
1458
SUZUKI, H.
0498, 1354, 1829
SUZUKI, K.
0633
SUZUKI, S.
0467

SVEDMYR, E.
1573
SVEJCAR, J.
1538
SVEJDA, J.
2484
SVERAK, L.
1105
SVET-MOLDASKY, G.YA.
1042
SVET-MOLDAVSKY, G.J.
0057, 0144, 0145
SVOBODA, D.
0024, 2114
SVOBODA, J.
0201
SWANBECK, G.
0997
SWANSON, D.H.
2230
SWANSON, S.A.V.
1853
SWEARINGEN, G.R.
2410
SWEET, W.H.
1991
SWETLY, P.
1092
SWIFT, M.
2534
SWISHER, S.L.
1688
SYDOW, G.
0739, 1811
SYPOWICZ, D.
0621
SZABO, G.
0335*
SZABO, I.
0422
SZABO, J.
0422
SZANTO, J.
1909
SZENDE, B.
0816
SZUCS, J.
0333*
TABARES, E.
0554
TAGUCHI, F.
1515
TAGUCHI, S.
2293
TAHARA, E.
1172
TAJIMA, F.
0509
TAKADA, A.
2275
TAKADA, M.
0151
TAKADA, Y.
2275
TAKADATE, A.
1355
TAKAHASHI, A.
0093, 0967

TAKAHASHI, H.
 0331
 TAKAHASHI, M.
 0095, 1044, 2324
 TAKAHASHI, T.
 0060, 0151
 TAKAMATSU, O.
 2251
 TAKANO, T.
 1784
 TAKASUGI, M.
 2442
 TAKAYAMA, S.
 0105, 0470, 2253
 TAKEBE, H.
 0489
 TAKEHARA, M.
 0657
 TAKEICHI, N.
 1533
 TAKEMOTO, K.K.
 1090, 1096, 2297.
 2376
 TAKEUCHI, J.
 1018
 TAKIGUCHI, T.
 2435
 TAKIZAWA, K.
 1453
 TAKIZAWA, S.
 0092
 TAKKAR, G.L.
 0889
 TAKKUNEN, J.
 0510
 TALAL, N.
 1932
 TALIB, H.
 0369
 TALLENT, M.G.
 1582*
 TALWALKAR, G.V.
 0969
 TANURA, M.
 1358
 TAN, E.M.
 0536
 TANABE, S.
 1028, 1063
 TANAKA, T.
 0605, 0727, 0949,
 1579
 TANAPONGPIPATANA, S.
 1766
 TANDY, K.K.
 2095, 2101
 TANI, E.
 0249, 1018
 TANK, R.
 1378*
 TANNOCK, I.F.
 0762
 TAPER, H.S.
 2080, 2247
 TARANCON MARTINEZ, A.
 0514*, 0742
 TARASOVA, G.V.
 0760

TARAYAMA, H.
 0431
 TARIKAS, H.
 2444
 TARKKANEN, J.
 0530
 TARNVIL, A.
 1571
 TAROCCO, R.P.
 0342*, 1760*
 TASCA, C.
 0480, 1349
 TASHJIAN, A.H., JR.
 1638
 TASSI, G.C.
 1506
 TATRA, G.
 2137
 TAURASO, N.M.
 1480
 TAYLOR, A.I.
 0806
 TAYLOR, C.M.
 1635
 TAYLOR, D.O.
 2039
 TAYLOR, D.O.N.
 2288
 TAYLOR, G.
 1131
 TAYLOR, G.N.
 1003
 TAYLOR, H.B.
 0287, 0743
 TAYLOR, J.R.
 1166
 TAYLOR, M.W.
 2526
 TAYLOR-PAPADIMITRIOU,
 1959, 2390
 TCHOU, H.P.
 2510
 TEEBOR, G.W.
 1299
 TEETS, K.
 0184
 TEITZ, Y.
 1447
 TEIXEIRA-PINTO, A.A.
 0243*
 TELLER, M.N.
 2188
 TELLES, N.C.
 0663
 TEMIN, H.H.
 0641, 0647, 1268,
 1945, 2358, 2368
 TEMPLETON, A.C.
 1609, 2492, 2493
 TEOFOLI, B.
 0341*
 TERADA, Y.
 0509
 TERAS, L.E.
 1814
 TERAYAMA, H.
 0056, 0432, 1138,
 2211

TEREBUS-KEKISH, O.
 0785
 TEREENTIEVA, E.I.
 2574*
 TER-GRIGOROV, V.S.
 1075, 1448, 14
 2323
 TERNBERG, J.L.
 0042
 TERNER, J.Y.
 0301*
 TERNI, M.
 0002
 TERRACINI, B.
 0962
 TESSMER, C.F.
 1257
 TESTA, M.C.
 0962
 TEUTSCH, B.
 1527
 TEVETHIA, S.S.
 1455, 1457, 23
 2449
 TEXIER, J.L.
 2108
 THEILEN, G.H.
 1872, 1874
 THEODOSSIOU, A.
 1818
 THEOLOGIDES, A.
 1139
 THIJS, L.G.
 0713
 THIRY, L.
 0167
 THOMAS, D.S.
 2459
 THOMAS, C.
 0031, 1343, 18
 1823
 THOMAS, E.D.
 1201
 THOMAS, G.M.
 0980
 THOMLEY, M.W.
 0825*
 THOMPSON, J.H.
 0502
 THOMPSON, M.
 1770
 THOMSON, S.
 1902
 THOR, D.E.
 2440
 THORBURN, M.J.
 0719
 THORNECROFT, I.H.
 1993
 THORNTON, J.
 1391
 THORNTON, R.
 0216
 THURSTON, O.G.
 1661
 THZULOV, C.
 0996

ICHO, U.
 1213
 IER, A.
 0233
 ILGEN, W.
 2026
 ILLSON, S.A.
 1993
 ILLY, R.
 1104
 IMBRELL, V.
 1610
 IMOFEYEV, V.T.
 1048, 1050
 ING, R.C.
 0792
 ING, R.C.Y.
 1950, 1962
 LCLKA-PLUSZCZYK, J.
 0946
 ODARIO, G.J.
 0150
 ODARO, G.J.
 0199, 0557, 0589,
 1037, 2320, 2370
 ODD, E.F.
 1347
 ODD, R.
 1141*
 OGNELLA, S.
 0733*
 OKUDA, S.
 1001
 OKUHARA, M.
 2141*
 OKUNO, S.
 0606
 OKUZEN, R.
 1357
 OLOT, F.
 1370, 1374*
 OMAS, V.
 0768*
 OMASULO, J.
 2569
 OMATIS, L.
 0476
 OMINAGA, K.
 0715
 OMINAGA, T.
 1791
 OMINGAS, R.
 0069, 0936
 OMIYASU, T.
 1398, 1399
 OMKINS, G.M.
 2078
 ONI, R.
 0552
 ONOMURA, A.
 1008
 ONTI, R.
 0341*
 OOLAN, H.W.
 0210, 1099
 ORGERSEN, O.
 0064

TORPIER, G.
 1079
 TORRES, F.O.
 2135
 TOT, F.
 2367
 TOTH, B.
 0100, 0437, 0513*
 1361
 TOTH, F.D.
 0335*
 TOURNIER, P.
 2157
 TOUSIMIS, A.J.
 1635
 TOYA, R.E., SR.
 0080
 TOYOSHIMA, K.
 0640, 1312, 1478
 TRAHAN, E.
 0704, 1985
 TRAININ, N.
 2276, 2278, 2430
 TRAININ, Z.
 2013
 TRALKA, T.S.
 2341
 TRAUB, F.
 0253
 TRAU, K.A.
 1023
 TRAVNICEK, M.
 0141, 0142, 0553
 TREGER, A.
 1795
 TREHEUX, A.
 1601*
 TRENDELENBURG, F.
 0750
 TRENTIN, J.J.
 0617, 1417, 1868,
 2343, 2431
 TREPEL, F.
 1754*
 TRIBUKAIT, B.
 2531
 TRIDENTE, G.
 1970
 TRILLING, D.
 1094
 TRITSCH, G.L.
 1673
 TRKULA, D.
 0666, 1951
 TROLL, W.
 0059, 0398
 TRONCALE, F.
 2076
 TRUJILLO, J.M.
 1257, 1969
 TSUBURA, Y.
 1312
 TSUCHIMOCHI, T.
 1650
 TSUCHIMOTO, T.
 0541, 1398, 1399
 TSUCHIYA, E.
 2106

TSUIKI, S.
 2086
 TU, S.M.
 0151
 TUBIANA, M.
 1011
 TUELER, K.
 2587*
 TUMILOWICZ, J.J.
 1869
 TUNG, H.T.
 0916
 TURCANU, P.
 0983
 TURKEVICH, N.M.
 1794
 TURKINGTON, R.W.
 2062, 2506
 TURKIYA, N.B.
 2196
 TURNER, H.C.
 0562, 1888, 2413
 TURNER, M.A.
 2145*
 TURNER, W.
 0602, 1069, 1933
 TUROSKA, B.
 2023*
 TURPIN, J.
 2031*
 TURUSOV, V.S.
 2219
 TUTTLE, N.
 0195
 TWEEDALE, D.N.
 0313
 TYE, C.Y.
 1165
 TYIHAK, E.
 0816
 TYNDALL, R.L.
 0174, 1348
 TYROLER, H.A.
 0276
 TYRRELL, S.A.
 2306
 UBERTINI, T.
 0157, 0158
 UCHIKAWA, T.
 0022
 UCHINO, H.
 0541
 UCHIYAMA, K.
 1639
 UEBERHORST, P.J.
 1871
 UEKAMA, K.
 1355
 UETANI, T.
 1560
 UHLENDORF, C.P.
 0953
 UHR, J.W.
 2009
 ULFELDER, H.
 1831
 ULLAND, B.
 2263

ULLYOT, J.L.
 0774
 UMANSKY, Y.A.
 0943
 UNGER, E.
 1407*, 2279
 UNGLAUB-LEISTEN, I.
 1879
 UPITER, M.Z.
 2472
 URBACH, F.
 1860
 USHIJIMA, K.
 0306, 1682
 USHIJIMA, R.
 1903
 USHIJIMA, R.N.
 1838
 US-KRASOVEC, M.
 0262*
 USSERY, M.A.
 2400*
 USTACELEBI, S.
 2327
 UZUNOV, P.
 2139
 VAAGE, J.
 2425
 VACZI, L.
 0335*, 1493
 VADLAMUDI, S.
 2448
 VAGNER-CAPODANO, A.M.
 0343*
 VAGNONI, G.
 0383*
 VAHERI, A.
 1755*
 VAHRSON, H.
 2034*
 VAIDYA, A.B.
 1419
 VAISHNAV, V.P.
 2038
 VAITKEVICIUS, V.K.
 2460
 VALAORAS, V.G.
 1187
 VALENTIN, F.
 1601*
 VALET, G.
 1387
 VALLADARES, Y.
 0554, 1501
 VALYI-NAGY, T.
 0422
 VANDENDRIESSCHE, P.
 0873*
 VANDEPUTTE, M.
 0685, 0883*, 2454
 VAN DER MAATEN, M.J.
 0563, 1875
 VAN DER MEER, J.
 2556
 VAN DER WATT, J.J.
 0402, 2135
 VAN DER WERF-MESSING,
 2116

VAN DE WIELE, R.L.
 1743
 VAN DUUREN, B.L.
 1291, 2204
 VAN GANSE, W.
 0981
 VAN GELDER, G.
 0403
 VANGHEEL, V.
 0544
 VAN HOOSIER, G.L., JR.
 0617, 1868
 VANHOUTTE, J.J.
 0827*
 VAN KAICK, G.
 0366
 VANKY, F.
 2418
 VAN NIE, R.
 2112
 VAN SLYCK, E.J.
 1247
 VANSOVER, A.
 1519
 VAN VUNAKIS, H.
 2089
 VAN WOERT, M.H.
 0567
 VARDOSANIDZE, E.SH.
 0618, 1050
 VARET, B.
 0165
 VARGA, L.
 0700
 VARICH, N.A.
 1038
 VARROY, A.
 1159
 VARTERESZ, V.
 0700
 VASCONCELOS-COSTA, J.
 0177
 VASIL'YEVA, N.H.
 2189
 VASS, W.
 1326
 VAUGHAN, J.
 1012
 VAUGHAN, R.K.
 2337
 VEAZEY, R.A.
 1301
 VEBERT, A.
 0495
 VEENEMA, R.J.
 2572
 VEHASKAKI, A.
 1595
 VELAZQUEZ, G.
 1188
 VENABLES, C.W.
 0777
 VENKATESAN, N.
 0466, 0474
 VENKITASUBRAMANIAN, T.A.
 0920, 1311
 VEPREK, L.
 1890

VERGER, C.
 0587, 1026
 VERHAEGHE, M.
 0747*
 VERHULSDONK, C.A.H.
 0990*
 VERMEIL, C.
 0705
 VERMIGLIO, G.
 2033*
 VERNEKER, S.D.
 1072, 1120
 VERNON, L.
 1688
 VESCO, C.
 1513, 2570
 VESSELINOVITCH, S.D.
 0492, 0496, 64
 VETROVA, E.P.
 0943
 VETTO, R.M.
 1324
 VIALE, E.
 2087
 VIALE, G.L.
 2087, 2523
 VIANNA, N.J.
 2019
 VICENTE, J.
 0381*, 0869*
 VICH, Z.
 0768*
 VICKERS, R.F.
 0244
 VIDI, I.
 0251
 VIEGAS, O.A.C.
 1609
 VIELKIND, J.
 2559
 VIELKIND, U.
 2559
 VIGIER, P.
 0020*
 VIGIL, E.L.
 2545
 VINCENT, M.M.
 0745
 VINCENT, P.C.
 0008, 1206
 VINOGRAD, J.
 1492, 1494
 VIOLA, P.L.
 2200
 VIRELLA, G.
 2007
 VISFELDT, J.
 1220, 2531
 VIVAR, G.
 1188
 VIZA, D.
 1141*
 VLAEMINCK, M.N.
 0493, 0495
 VLAHAKIS, G.
 0631, 1067, 14
 1695

ASOV, N.N.
 0948
 CEK, B.
 2465*
 DELKEL, E.F.
 1638
 OGEL, A.
 0558
 OGEL, C.L.
 0723
 OGEL, H.H., JR.
 0532
 OGT, P.K.
 0202, 0640, 0649,
 1066, 1439, 1478,
 2359, 2366
 OLEGOV, A.I.
 2022*, 2232
 OLFSO, N.I.
 0487, 0853
 OLGAREV, M.N.
 2471
 OLKERS, S.A.S.
 2526
 OLM, M.
 0408
 ON ESSEN, C.F.
 1612
 ONKA, V.
 1060, 1509, 1532,
 1538, 1923
 ORONIN, E.S.
 2166*
 OUTE, P.A., JR.
 2556
 REDEVOE, D.L.
 1035
 UOPALA, U.
 0510
 YSHESLAVOVA, M.YA.
 0025
 WACHSMANN, F.
 0370
 WACKER, A.
 1551
 WADDELL, A.
 0674, 0683
 WELBROECK-VAN GAVER, C.
 0930
 WAGGONER, D.E.
 1434, 1578, 1617
 WAGNER, E.K.
 0621, 1058
 WAGNER, G.
 2053*
 WAGNER, H.P.
 1242
 WAGNER, J.C.
 1610
 WAGNER, J.L.
 1540
 WAGNER, K.H.
 0912
 WAGNER, L.
 2205
 WAGNER, R.
 1815

WAGNER-HERING, E.
 0912
 WAHLQUIST, L.
 1645
 WAHREN, B.
 0599
 WAINFAN, E.
 2304
 WAISSBLUTH, J.G.
 1228
 WAKABAYASHI, K.
 2546
 WAKONIG-VAARTAJA, T.
 0809
 WALBORG, E.F., JR.
 0429
 WALBURG, H.E., JR.
 0174
 WALDENSTROEM, J.
 0832
 WALES, J.H.
 1308
 WALKER, D.L.
 2379
 WALKER, J.E.
 1758*
 WALKER, K.R.
 0104
 WALL, A.J.
 0740
 WALLACE, A.C.
 1683
 WALLACE, C.
 1588
 WALLACE, H.A.
 1116
 WALLACE, J.H.
 2340
 WALLACE, W.C.
 0419
 WALLCAVE, L.
 1330
 WALLER, J.M.
 1108
 WALTERS, M.N.I.
 2316
 WALTON, M.F.
 0902
 WANG, C.H.
 0151
 WANG, F.C.
 1353
 WANG, R.
 1507, 2388
 WARD, F.E.
 1542
 WARREN, J.
 2366
 WARREN, L.
 1939, 1957
 WARTENBERG, J.
 2576*
 WARWICK, O.P.
 0081, 0396, 0971
 WASSERMAN, M.B.
 0909
 WATANABE, I.
 0572

WATANABE, M.
 1966
 WATANABE, T.
 2415
 WATANBE, K.
 1771
 WATCHI, J.M.
 1371
 WATNE, A.L.
 0228
 WATRACH, A.M.
 1151
 WATSON, C.J.
 1572, 1702
 WATSON, D.H.
 1462
 WATSON, F.R.
 0308
 WATSON, K.
 0141, 0142, 0553
 WATSON, T.A.
 0318
 WATTENBERG, L.W.
 0070, 1332
 WAUBKE, R.
 0004
 WAYSS, K.
 0408
 WEBB, D.
 2403
 WEBB, T.E.
 2262
 WEBER, A.F.
 1877
 WEBER, E.
 1405*
 WEBER, G.
 2498
 WEBER, G.H.
 1892, 1893, 2082
 WEBER, J.
 0611
 WEDDERBURN, N.
 0600, 0610
 WEE, R.
 0232
 WEEKS, J.L.
 0111
 WEGENER, K.
 1397
 WEGNER, K.W.
 1613
 WEI, L.S.
 0519*
 WEI, R.D.
 2206
 WEIGAND, K.
 0305
 WEIL, R.
 0676
 WEILER, O.
 1436
 WEINBERGER, M.
 1792
 WEINER, L.M.
 1126
 WEINER, N.D.
 1338

WEINREB, S.M.
 1310
 WEINSEN, U.
 0305
 WEINSTEIN, E.B.
 2199
 WEINSTEIN, I.B.
 2090
 WEINTRAUB, B.D.
 1656
 WEISBURGER, E.K.
 0409, 2255, 2263
 WEISBURGER, J.H.
 0041, 0054, 0409,
 2255, 2263
 WEISS, D.W.
 0894, 1558, 1927,
 2402
 WEISS, J.F.
 0089
 WEISS, L.
 1247, 1433
 WEISS, K.
 1083
 WEISS, R.A.
 0814
 WEISS, W.
 0764, 1626
 WEISSBACH, A.
 2561
 WELCH, R.M.
 1796
 WELLER, D.L.
 1563
 WELLER, W.
 1768
 WELLINGS, S.R.
 1144
 WELLS, R.T.
 2368
 WELSCH, C.W.
 0770, 0929
 WENNERSTRAND, J.
 1007
 WENYON, C.E.M.
 0086, 0087, 0476
 WENZ, W.
 0366
 WEPSIC, H.T.
 1555, 1992
 WERTELECKI, W.
 0012
 WERTHAMER, S.
 0884
 WERNER, W.
 2578*
 WESSEL, W.
 1679
 WESSLEN, T.
 1093
 WESTBURY, G.
 0847
 WESTFALL, B.B.
 1143
 WETTELAND, P.
 2054*
 WETTER, O.
 0226

WETTIG, K.
 0401
 WETZEL, R.
 1851
 WEWER, B.
 0874*
 WEXLER, M.R.
 1558
 WHALLEY, J.M.
 1440
 WHANG-PENG, J.
 0576, 0798, 1512,
 1871, 1883
 WHIMSTER, I.W.
 2396*
 WHITE, A.
 0197
 WHITE, D.A.
 1504
 WHITE, D.F.
 0318
 WHITE, H.J.
 2555
 WHITE, J.E.
 0273
 WHITE, L.L.
 2192
 WHITE, W.L.
 1071, 2399*
 WHITFIELD, J.F.
 0618
 WHITMIRE, R.E., JR.
 0301*
 WHITMORE, W.F.
 0746
 WHITWELL, F.
 1858
 WIEBEL, F.
 0445
 WIED, G.L.
 2045
 WIEGENSTEIN, L.
 1378*
 WIENER, F.
 2386, 2554
 WIENER, F.P.
 1046
 WIENER, M.
 2447
 WIERNIK, G.
 2109
 WIESE, W.H.
 1052
 WIESSLER, M.
 0082
 WILBANKS, G.D.
 0620
 WILBERT, S.M.
 1432
 WILDNER, G.P.
 2215
 WILKINSON, R.
 2088, 2474
 WILLIAMS, A.E.
 1668
 WILLIAMS, A.O.
 0955

WILLIAMS, E.A.
 2109
 WILLIAMS, G.
 1647
 WILLIAMS, H.R., JR.
 0054
 WILLIAMS, J.F.
 1053, 2327, 238
 WILLIAMS, R.C., JR.
 1139
 WILLIAMS, R.E.O.
 1189
 WILLIAMS, S.N.
 0919
 WILLIAMS, W.C.
 2410
 WILLIAMS, W.J.
 1253
 WILLIAMSON, M.E.
 1059
 WILLIS, R.A.
 1846
 WILSON, H.
 1258
 WILSON, P.D.
 2500
 WILSON, R.
 2242
 WILSON, S.
 0783
 WILSON, S.M.
 2512
 WIMBERLY, I.
 1885
 WINE, S.S.
 1860
 WINETROUT, M.
 0191
 WINOCOUR, E.
 1103, 1499
 WINSHIP, T.
 1173
 WINTERS, A.L.
 1112
 WINTERS, D.
 0181
 WISEMAN, S.
 0738
 WITHERS, H.R.
 0524
 WITTER, R.L.
 0161, 1465
 WITTIG, G.
 2215
 WITZ, I.P.
 1133, 2441
 WIVEL, N.A.
 0171, 1422
 WLODARSKI, K.
 1415
 WOGAN, G.N.
 0046, 0428, 131
 1744, 2207
 WOLBERG, W.H.
 1545, 2452
 WOLF, M.
 2238

OLFE, L.G.
 1872
 OLMAN, S.
 0558
 ONG, Y.C.
 1209
 OOD, M.
 1300
 OOD, W.C.
 0704, 2016
 OODE, G.N.
 1031
 OODHAM, A.A.
 0387*
 OODING, W.L.
 1777
 OODS, D.A.
 0456
 OODS, M.W.
 1143
 OODS, W.A.
 0171, 1036
 OODSIDE, N.J.
 1420
 OOKROOF, J.G.
 0386*
 OLAM, G.L.
 1700
 OLF, C.R.
 0975
 OLUM, J.C.
 0042
 ORTHINGTON, M.
 1528
 OIGHT, B.S.
 0175
 OIGHT, D.H.
 0689*
 OIGHT, P.D.
 0777
 O, C.
 2557
 O, S.Y.
 1783
 OLFF, U.C.
 2530
 ODERLICH, J.R.
 1559
 ODERLICH, V.
 1426
 OATT, A.P.
 0337*
 OCHULIS, A.R.
 1700
 OKE, J.
 2385
 ODER, E.L.
 0286, 0850, 0935,
 0977, 2260
 ODHAM, N.
 1245
 ONG, M.D.
 0433
 OBE, Y.
 1017
 OBLONSKAYA, L.YA.
 2220

YABLONSKI, M.
 2485
 YAGI, Y.
 2415
 YAGIHASHI, H.
 1983
 YAKOVLEVA, L.A.
 1867
 YAKOVLEVA, L.S.
 1475, 2169*
 YALCINER, S.
 0899
 YAM, L.T.
 1637
 YAMADA, K.
 1560
 YAMADA, S.
 0040
 YAMADA, T.
 2293
 YAMAGATA, S.
 1639, 2058
 YAMAGUCHI, J.
 1020
 YAMAHA, T.
 1771
 YAMAMOTO, G.
 1080
 YAMAMOTO, H.
 1489, 1978
 YAMAMOTO, K.
 2292
 YAMAMOTO, N.
 0489
 YAMAMOTO, R.S.
 0041, 0054, 0409,
 2255
 YAMAMOTO, S.
 1098
 YAMAMOTO, T.
 0633, 0653, 1172,
 1398, 1453
 YAMANE, I.
 1241
 YAMANE, Y.
 0096
 YAMANOUCHI, K.
 2446
 YANAGISAWA, M.
 1121
 YANAI, R.
 0312, 0927, 1207
 YANG, C.S.
 0151, 1972
 YANG, H.Y.
 0324
 YANG, S.J.
 2201
 YANG, S.S.
 0792
 YANG, W.K.
 2504
 YARBRO, J.W.
 1643
 YARDLEY, J.H.
 1714*
 YASHPHE, D.J.
 2159

YASUZUMI, G.
 0430
 YATA, J.
 1121
 YATES, V.J.
 0182, 0208, 1459
 YEE, M.
 1337
 YEGHIAYAN, E.
 0925, 1319
 YERGANIAN, G.
 1828
 YERMOLOVA, T.S.
 1586
 YOKORO, K.
 0092, 0604
 YOKOTA, Y.
 1587
 YOKOYAMA, T.
 1784
 YOON, C.H.
 2422
 YORAN, C.
 1615
 YOSHIDA, H.
 1414
 YOSHIDA, K.
 0306, 1682
 YOSHIDA, O.
 0038
 YOSHIDA, T.
 0151
 YOSIDA, T.H.
 0098, 0102
 YOSHIDA, T.O.
 2381
 YOSHIDA, Y.
 1515
 YOSHII, S.
 0649
 YOSHIKAWA-FUKADA, M.
 2164*
 YOSHIKURA, H.
 0198, 1452, 1937
 YOSHIMURA, Y.
 2381
 YOST, Y.
 2183
 YOUN, J.K.
 2416
 YOUNG, E.M.
 0050, 1317
 YOUNG, L.
 1530, 2402
 YOUNG, P.C.
 0746
 YOUNG, S.
 0442
 YOUNKERS, P.E.
 0953
 YU, C.K.
 0129
 YU, M.
 0232
 YUASA, S.
 1187
 YUMOTO, T.
 0561, 0569

YUSHOK, W.D.
 2065
 YUSPA, S.H.
 0931, 0934
 ZABELZHINSKIY, M.A.
 1289
 ZABEZHINSKY, M.
 0023
 ZACHARIA, T.P.
 1468
 ZADOK, S.
 0465
 ZADOROZHNIAYA, N.A.
 0972
 ZAHMERT, R.
 1397
 ZAIN-UL-ABEDIN, M.
 0022
 ZAJDELA, F.
 0411
 ZAJICEK, J.
 0262*
 ZAK, M.
 0405
 ZALDIVAR, R.
 0532, 1169, 2037
 ZAMBERNARD, J.
 0567
 ZAMCHECK, N.
 0362
 ZAMECNIK, P.C.
 2147
 ZANETTI, M.
 0583
 ZANG, K.O.
 1692, 2532
 ZANK, M.
 2516
 ZANKL, H.
 1692, 2532
 ZANSTRA, R.
 0283
 ZAUCHE, A.
 1628*
 ZAPOL'SKAYA, N.A.
 2294*

ZAPSEPIN, N.I.
 0686*
 ZARAFONETIS, C.J.D.
 0310
 ZARIDZE, D.G.
 2030
 ZASYPKA, A.T.
 0732*, 0911
 ZATSEPIN, N.I.
 1526
 ZAUN, H.
 0787
 ZAVADIL, M.
 0227
 ZAVADOVA, H.
 1509, 1538
 ZAWARIKA, M.
 2576*
 ZAWIRSKA, B.
 2190
 ZBAR, B.
 0727, 1555, 1922,
 2440
 ZBYTNIIEWSKI, Z.
 1283*
 ZEIGEL, R.F.
 1425, 1430
 ZEIKUS, J.G.
 2526
 ZELLDADT, I.
 0175, 0626, 0630,
 1420
 ZEMBALA, M.
 1510
 ZEMER, D.
 1615
 ZENKER, N.
 2064
 ZEPPA, M.P.
 1456, 2326
 ZERVAS, J.D.
 0717
 ZETERBERG, A.
 0813
 ZEVE, V.
 0589, 1871

ZHAROVA, YF.I.
 2319
 ZHILEVICH, A.V.
 1473
 ZHUDINA, A.I.
 0560
 ZIANTL, F.
 0712
 ZIEBARTH, D.
 2215
 ZIEGLER, J.L.
 1973, 2493
 ZIELINSKI, J.
 1600*
 ZIEVE, F.J.
 1773
 ZIL'FYAN, V.H.
 0453
 ZIMMER, S.
 1662
 ZIMMERMAN, J.
 2329
 ZIMMERMAN, J.E., JR.
 1047
 ZIMMERMANN, F.K.
 0412, 2177*
 ZINTEL, H.A.
 1591
 ZINTL, F.
 1738
 ZISBLATT, M.
 0197
 ZIVY, P.
 1834
 ZIZKA, J.
 0799
 ZOUPANOS, G.
 0360
 ZSCHIESCHE, W.
 2272*
 ZUCKERMANN, C.
 1195*
 ZUR HAUSEN, H.
 0574
 1752*

SUBJECT INDEX

ACETAMIDOFLUORENE

BILE DUCT LIGATION, N-HYDROXY-2-
ACETAMIDOFLUORENE, ADRENALECTOMY
(0908)
ETOTOLUIDIDE
AMINOBENZOIC ACID, N-2-FLUORENYLACETA-
MIDE, CARCINOGEN-INHIBITOR (0041)
ACETOXYACETAMIDOFLUORENE
2-(N-HYDROXY)ACETAMIDOFLUORENE,
PHOSPHATE ESTER, ULTIMATE
CARCINOGEN (0909)
ACETOXY-2-ACETYLAMINOFLUORENE
DNA, BINDING (1772)
DNA, POLYNUCLEOTIDES (1774)
TRNA, GUANOSINE (2199)
ACETYLAMINOFLUORENE
DERIVATIVES, RADIOACTIVE PRECURSOR
INCORPORATION, RNA AND DNA SYNTHESIS
(0408)
DIETARY INDOLE, URINARY BLADDER
TUMORS (0907)
HEPATOMA, RESISTANCE, RAT (2426)
LIVER CARCINOMA, PORPHYRINS,
RAT (2190)
METABOLITE, BINDING, RAT LIVER,
NUCLEIC ACIDS (1301)
MOUSE, BLADDER, EPITHELIUM (1300)
NITRITE, ANTICARCINOGEN, FREE RADICAL
(0042)

HALASIA

CARCINOMA, ESOPHAGUS (1700)
TINOMYCIN D
DNA SYNTHESIS, SV40 VIRUS (0662)
INVASIVE ABDOMINAL CARCINOMA (0024)
MAMMARY TUMOR SUPPRESSION,
7,12-DIMETHYLBENZ(A)ANTHRACENE
(0932)
PUROMYCIN, LYMPHOCYTES, PHYTO-
HEMAGGLUTININ (1678)

ENOCARCINOMA

BREAST CANCER, 7,12-DIMETHYLBENZAN-
THRACENE, ESTROGEN, RAT (0064)
CERVIX UTERI, CHROMOSOMES (0254)
COLON, CARCINOEMBRYONIC ANTIGEN,
LOCALIZATION (0235)
COLON, URETEROSIGMOIDOSTOMY, MAN
(0825)*
EMBRYONAL, TESTS, CHILDREN (0746)
ENDOMETRIUM, PROTEIN SULFHYDRYL
GROUPS, HUMAN (2466)
FERTILITY, ENDOMETRIAL HYPERPLASIA (0743)
IMMUNOSUPPRESSION, THYMECTOMY,
RADIATION, MICE (1552)
METASTASIS, THYROID, HUMAN (0823)
NASAL SYSTEM, WOOD DUST (0113)
PAPILLARY, GENETIC PREDISPOSITION,
FAMILIAL OVARIAN CARCINOMA (0808)
THYROID, IODINE 131 (0126)

ENOMA

BRONCHO-ALVEOLAR CANCER, SHEEP (0820)
GASTRIC, N-METHYL-N-NITROSO-N'-
ACETYLUREA, RAT (0483)
LUNG, URETHAN, RADIATION (0101)
MALIGNANT, THYROID, X-RAY (0135)
OLESCENCE
MAMMARY FIBROADENOMAS (1705)
RAPID BONE GROWTH, ACUTE MYELOID
LEUKEMIA (0375)

ADRENAL GLAND

ADRENALECTOMY, BILE DUCT LIGATION,
N-HYDROXY-2-ACETAMIDOFLUORENE
(0908)
ADRENOCORTICAL VIRILIZING CARCINOMA,
STEROIDS (1642)
CARCINOMA, CUSHING'S SYNDROME,
BILATERAL HYPERPLASIA, HORMONAL
THERAPY (0741)
CARCINOMA, FISSION NEUTRON IRRADIATION
(0532)
CARCINOMA, HUMAN, STEROID ANALYSIS
(0782)
CORTEX, LIPID HYPERPLASIA, ANILINE,
RAT (0925)
CORTICAL CARCINOMA, ESTRADIOL,
RAT (0890)
ENDOCRINE LESION, URETHANE (0498)
ESTROGEN-DEPENDENT CARCINOMA,
RNA AND DNA METABOLISM (1770)
HISTOCHEMISTRY, WHOLE BODY
IRRADIATION, RAT (1407)*
MEDULLA, PREOPTIC-ANTERIOR HYPO-
THALAMIC LESION, GANGLIONEUROMA, RAT
(1259)
NECROSIS, 7,12-DIMETHYLBENZ(A)ANTHRA-
CENE, RAT (0438)
NEUROBLASTOMA, ANTIGENS, FETUS,
(1577)
POSTCASTRATIONAL ADRENAL TUMORS,
STRAIN VARIABILITY, MICE (1199)

ADRIAMYCIN

BLASTOGENESIS IN HUMAN LYMPHOCYTES,
MUTAGENESIS IN HUMAN LYMPHOCYTES
(0699)

ADSORPTION

ADENOVIRUS TYPE 7, ERYTHROCYTE (0614)

AFLATOXIN

ACID PHOSPHATASE, LYSOSOMAL ENZYME
ACTIVITY, CHICKEN (0916)
ANALYTICAL METHODS, REVIEW (0881)*
ASPERGILLUS FLAVUS, EFFECT OF
TEMPERATURE (0519)*
B, LIVER NUCLEAR RNA, RNA POLYMERASE,
RAT (0046)
B, LYMPHOCYTE TRANSFORMATION, PHYTO-
HEMAGGLUTININ (0045)
B1, ACUTE TOXICITY, KUPFFER CELL
HYPERPLASIA, BILE DUCT EPITHELIUM,
HAMSTER (0517)*
B1, B2, G1, G2, ANIMAL FEEDS (0991)*
B1, B2, G1, G2, COUMARINS, FURAZOLIUM,
GUINEA PIG, HYPERSENSITIVITY (0424)
B1, CHICK LIVER, CARBOHYDRATE
METABOLISM (1311)
B1, DNA LIVER, RATS (0427)
B1, ENZYME HISTOCHEMISTRY, MUCOR
HIEMALIS FUNGUS (1376)*
B1, HEPATECTOMY, RNA SYNTHESIS,
LIVER, RAT (2205)
B1, KIDNEY, RNA POLYMERASE,
MOUSE (2207)
B1, LABELED ACETATE INCORPORATION,
HUMAN SKIN LIPIDS (0918)
B1, LIVER CARCINOMA,
HEPATECTOMY, RAT (2210)
B1, LIVER MICROSOME, REPTILE, FOWL
(1309)

- B1, LIVER NUCLEIC ACID SYNTHESIS, PHENOBARBITAL (0919)
 B1, MICROSOMAL HYDROXYLASE, 3,4-BENZOPYRENE (0428)
 B1, MUTAGENESIS, DROSOPHILA (2208)
 B1, RAT LIVER, TRANSFORMATION, IN VITRO (1312)
 B1, REYE'S SYNDROME, TOXIC REACTION IN MONKEYS (1777)
 B1, RNA SYNTHESIS, LIVER CELLS (0914)
 B1, STRUCTURE-ACTIVITY RELATIONSHIP, TROUT (1308)
 B1, TWO DIMENSIONAL THIN LAYER CHROMATOGRAPHY, FOOD PRODUCTS, PEANUTS (0990)*
 BEAGLE, LIVER CHANGES (1778)
 BIOSYNTHESIS, METHIONINE ANALOGS (2267)*
 CIRRHOSIS, CARCINOGENESIS, LIVER, RAT (2206)
 DIETARY, LIVER INJURY, RHESUS MONKEY (0426)
 DNA, RNA, REVIEW (1744)
 G1, LIVER, RAT (2209)
 HEPATIC CHANGES, ENDOPLASMIC RETICULUM, MITOCHONDRIAL ATPASE, RATS (1780)
 LIPOTROPE-DEFICIENT DIET, LIVER TUMORS (0915)
 LIVER, ENZYME ACTIVITY, CITRIC ACID CYCLE (0920)
 METABOLISM IN LIVER, DEGRADATION PRODUCTS (0917)
 MYCOTOXINS, BLOOD MALIGNANCIES, LIVER CARCINOMA (1276)
 MYCOTOXINS, TUMORIGENESIS, REVIEW (0388)*
 NUCLEIC ACID SYNTHESIS, INHIBITION (0049)
 NURSING MILK, PIG, STUNTED GROWTH (0048)
 OILSEED PROTEINS, ANIMAL FEED, TOXICITY, REVIEW (0387)*
 PALMOTOXINS, EMBRYO LIVER (0425)
 PEANUTS, DIETETICS, REVIEW (0386)*
 P1, MONKEY, AFLATOXIN METABOLITE (1310)
 SWAZILAND, LIVER CARCINOMA (1781)
 TUMOR INDUCTION, NUCLEIC ACID BINDING (0047)
- AGE
 ADJUSTMENT, EPIDEMIOLOGY, MATHEMATICAL MODEL (0264)
 BENZO(A)PYRENE, ORGANOTROPY, HUMAN (1333)
 CARCINOMA, HORMONES, ANTIGENICITY (1740)
 CHRONIC THYROIDITIS, RAT, TRYPAN BLUE (0034)
 CORRELATION, LIVER, ALPHA-FETOPROTEIN (0231)
 7,12-DIMETHYLBENZ(A)ANTHRACENE, 3-METHYLCHOLANTHRENE, RAT, MOUSE (0436)
 DISTRIBUTION, HODGKIN'S DISEASE (1218)
 FIRST PREGNANCY, MAMMARY CARCINOMA, WEIGHT (1618)
- HODGKIN'S DISEASE, HISTOLOGY, TWO ENTITIES (0260)
 INOCULATION, MOUSE MAMMARY TUMOR VIRUS, MILK ANTIGEN ASSAY (0194)
 NEW ZEALAND MICE, MURINE SARCOMA VIRUS, TUMOR REGRESSION (1932)
 PERINATAL PERIOD, TUMOR PROFILE, URETHAN INDUCTION (0496)
 TEEN-AGE PATIENTS, CYTOLOGIC ATYPIA, CARCINOMA OF THE CERVIX (0744)
 TUMOR, EPIDEMIOLOGY, REVIEW (1725)
 TUMOR SPECTRUM, URETHAN (0492)
 TUMORIGENICITY OF MOUSE CELL LINES, IN VITRO NEOPLASTIC TRANSFORMATION (1229)
 URETHAN, TUMOR INDUCTION, HAMSTERS 1361
 VARIATION, RH NEGATIVITY, LEUKEMIA (0801)
 WOMEN, SURVIVAL RATE, MAMMARY CARCINOMA (0287)
- AGGLUTINATION
 TRANSFORMED CELLS, SIMIAN VIRUS 40, ADENOVIRUS TYPE 12, ORNITHINE, LEUCINE POLYMER (0661)
- AIR POLLUTION
 BRONCHOGENIC CARINOMA, EPIDEMIOLOGY, CZECHOSLOVAKIA (0768)*
 CARCINOGENS, BRONCHIAL CARCINOMA, HYDROCARBONS (0461)
 EPIDEMIOLOGY, LUNG CANCER (0016)
 LUNG CANCER, SMOKING, ITALY (0383)*
 LUNG CANCER MORTALITY, AUSTRALIAN IMMIGRANTS (2049)
 URBAN, CARCINOMA OF THE TONSIL, CANINE RESPIRATORY TRACT CARCINOMA (1183)
- ALDRIN
 TUMORIGENICITY, DIELDRIN, ENDRIN (0421)
- N-ALKYL-4-AMINOAZOBENZENE
 AZO DYE BINDING (0056)
- ALKYLATING AGENT
 CHLORAMBUCIL, BUSULPHAN, BONE MARROW CELL PROLIFERATION (2070)
 CYCLOPHOSPHAMIDE, CARCINOGENICITY, RAT, MOUSE (0906)
 N-DIAZOACETYLGLYCINAMIDE, N-DIAZOACETYLGLYCINE HYDRAZIDE, CARCINOGENICITY, MOUSE (0401)
 DNA, REPAIR SYNTHESIS, HELA, HAMSTER (2254)
 DNA, RNA, REPAIR, HELA (2248)
 1,3-PROPANE SULTONE, 1,4-BUTANE SULTONE, RATS, NEUROGENIC TUMORS (0905)
 THYMUS, DNA, THERMAL DENATURATION, CALF (0422)
 TRENIMON, MUTAGENESIS, HAMSTERS, BONE MARROW (0903)
- ALUMINUM
 4-NITROQUINOLINE 1-OXIDE, LUNG ADENOCARCINOMA (0096)
- AMELOBLASTOMA
 DENTAL CYST, JAW (0244)
 ODONTOGENIC TUMORS, ENZYME ACTIVITY (0784)

INOACETONITRILE
 METABOLISM, DIMETHYLNITROSAMINE
 (0961)
 NO ACID
 ACCEPTOR RNA, AVIAN MYELOBLASTOSIS
 VIRUS, AMINOACYLATION CAPACITY
 (0585)
 ALPHA-AMINOISOBUTYRIC ACID UPTAKE,
 IRRADIATED RAT LIVER (1386)
 ARGININE DEPRIVATION, POLYOMA
 VIRUS, INFECTION (1112)
 COMPOSITION, T-ANTIGEN, ADENOVIRUS
 TYPE 12, HAMSTER (1526)
 LEUKEMIC LYMPHOBLASTS, TRANSFER RNA
 (0790)
 LEUKOSIS, ANTIGEN, VIRUS (1027)
 NOAZOBENZENE
 N,N-DIMETHYL-4-AMINOAZOBENZENE,
 LIVER CELL NUCLEI RNA POLYMERASE,
 OTHER DERIVATIVES, RAT (1783)
 NOAZOTOLUENE
 ORTHO-, NUCLEIC ACID BINDING, PROTEIN
 BINDING (0028)
 AMINO-2',3-DIMETHYL-AZOBENZENE
 BINDING, LIVER PROTEIN, RAT (0432)
 TA-AMINOISOBUTYRIC ACID
 BLADDER CARCINOMAS (0336)*
 NOSTILBENE
 DERIVATIVES, EAR DUCT TUMOR, TRANS-4-
 DIMETHYLAMINOSTILBENE (0031)
 BONE MARROW, THYMUS, MITOSIS, RAT
 (0818)
 CELL SURFACE ALTERATIONS, ROUS
 VIRUS, POLYOMA VIRUS (1079)
 EMIA
 GASTRIC CARCINOMA, VITILIGO (0777)
 ILINE
 LIPID HYPERPLASIA, RAT ADRENAL CORTEX
 (0925)
 RAT CORPORA LUTEA, STEROIDOGENESIS
 (1319)
 TIBIOTIC
 BIOMYCIN, ORTHOAMINOAZOTOLUENE, LIVER,
 MOUSE (0025)
 EXORIBONUCLEASE, RNA, EHRLICH'S
 ASCITES TUMOR (2179)
 TIBODY
 ANTILYMPHOCYTE SERUM, LYMPHO-
 CYTES, SARCOMA, MICE (2442)
 ANTILYMPHOCYTE SERUM, SPON-
 TANEOUS LYMPHOMA, MOUSE
 (2431)
 ANTISARCOMA, HUMAN SARCOMA, VIRUS
 (1880)
 ANTISARCOMA, IMMUNITY, SKELETAL
 SARCOMAS (0710)
 4-AZOGUINOLINE-1-OXIDE,
 4-NITROQUINOLINE-1-OXIDE (1994)
 COMPLEMENT, EHRLICH'S ASCITES
 TUMOR, NORMAL HUMAN SERUM
 (2417)
 EPSTEIN-BARR VIRUS (0757)
 EPSTEIN-BARR VIRUS, BURKITT'S
 LYMPHOMA (1973)
 EPSTEIN-BARR VIRUS, BURKITT'S
 LYMPHOMA, TAIWAN MONKEY (1972)
 EPSTEIN-BARR VIRUS, CHILDREN (0758)

FELINE LEUKEMIA VIRUS, VIRAL ANTIGEN
 (0163)
 GROSS LEUKEMIA VIRUS, GLOMERULO-
 NEPHRITIS, MOUSE (1034)
 GROSS LEUKEMIA VIRUS, IMMUNO-
 FLUORESCENT FOCUS ASSAY (1036)
 HEMAGGLUTINATION, INFECTIVITY, RAT
 VIRUSES (0559)
 HERPES SIMPLEX VIRUS,
 PERSISTENCE, EARLE'S L CELLS,
 HUMAN (2334)
 HERPESVIRUS TYPE 2, INVASIVE
 CERVICAL CARCINOMA (0624)
 HETEROLOGOUS ANTIGLIOMA 'CARRIER',
 GLIOMAS, HUMAN (2018)
 HODGKIN'S DISEASE, EB VIRUS, HERPES
 SIMPLEX, CYTOMEGALOVIRUS (0155)
 IMMUNOGLOBULIN PRODUCTION, MURINE
 PLASMACYTOMA (1546)
 IMMUNOGLOBULINS, IGG, IGA (0229)
 LEUKEMIA STAGES, L1210, MOUSE
 (2448)
 MAMMARY GLAND TUMOR,
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 (1990)
 MONKEY KIDNEY, SV40, VIRUS REPLICATION
 (1495)
 MULTIPLE MYELOMA, KEYHOLE LIMPET
 HEMOCYANIN (1576)
 MURINE SARCOMA, TUMOR-SPECIFIC
 ANTIGEN, 3-METHYLCHOLANTHRENE (0072)
 MYELOMA, MOUSE TISSUE (2414)
 PARABLASTS, LEUKEMIA, CHILDREN,
 CONTACT PERSONS (0712)
 PLATELET LEUCOCYTE, TROPHOBLASTIC
 TUMORS, CHORIOEPITHELIOMA (0227)
 PRODUCTION, CANCER PATIENTS,
 17D YELLOW FEVER VIRUS VACCINE
 (1140)
 RESPONSE, GROSS LEUKEMIA VIRUS,
 LYMPHOMA (1520)
 SARCOMA, VIRUS, HUMAN (0147)
 SV40, LABORATORY MONKEY HANDLERS
 (1524)
 SV40, PREGNANT HAMSTERS (0213)
 TITERS, EPSTEIN-BARR VIRUS,
 MACAQUE MONKEYS (1974)
 TITERS, SURVIVAL TIME, CANCER
 PATIENTS, FLAGELLIN (1119)
 TITERS IN HODGKIN'S DISEASE, EPSTEIN-
 BARR VIRUS (1025)
 VIRUS, HUMAN SERA, EPSTEIN-BARR,
 HERPES (1063)
 ANTICARCINOGEN
 NITRITE, MECHANISM, FREE RADICAL,
 2-ACETYLAMINOFLUORENE (0042)
 ANTIGEN
 2-ACETYLAMINOFLUORENE,
 HEPATOMA, RESISTANCE, RAT
 (2426)
 ADENOVIRUS TYPE 12, HELA CELL
 (1981)
 ADENOVIRUS TYPE 12 SARCOMA, HAMSTER
 (0618)
 AMINO ACID, LEUKOSIS, VIRUS (1027)
 ANTIGENIC ANALYSIS, L STRAIN MOUSE
 CELLS, MURINE LEUKEMIA-ASSOCIATED
 (0165)

ANTI-MOUSE EGG, CYTOTOXICITY, SV40 (0669)
 AUSTRALIA, PRIMARY LIVER CANCER (0724)
 CANCER TEST, BASIC PROTEIN, LYMPHOCYTE SENSITIZATION (1197)
 CARCINOEMBRYONIC, REVERSION, HUMAN (2172)*
 CARCINOMA, HORMONES (1740)
 CARCINOEMBRYONIC, COLON, ADENOCARCINOMA, LOCALIZATION (0235)
 CARCINOEMBRYONIC, ALPHA-FETOPROTEIN, GASTROINTESTINAL TRACT CANCER, HEPATOMA, TERATOMA (0240)*
 CARRIER AGENTS, TUMOR VACCINES (0356)
 CELL MEMBRANE, SV40, KIDNEY (2447)
 CELL-SURFACE, SARCOMAS, HUMAN (2016)
 CHICK-EMBRYO-LETHAL-ORPHAN VIRUS, CHICK KIDNEY CELLS (1417)
 CHICKEN FEATHER FOLLICLES, MAREK'S DISEASE HERPESVIRUS (1965)
 CHORIOCARCINOMA, PLACENTA, KIDNEY (2014)
 COMMON ANTIGENICITY, ANEMIA-INDUCING PLACENTAL SUBSTANCE, MUCOPROTEIN IN URINE OF CANCER PATIENTS (1575)
 COMMON ANTIGENICITY, MAMMARY TUMOR VIRUS, MOUSE (1536)
 COMPLEMENT FIXATION, HEMAGGLUTINATION REACTION, MURINE LEUKEMIA VIRUSES (1909)
 COMPLEX, AVIARY SARCOMA, ROUS SARCOMA VIRUS (1527)
 CROSS-REACTIVITY, MAREK'S DISEASE, EPSTEIN-BARR VIRUS, HERPESVIRUS (1466)
 DEN-86, HEPATOMA, DIETHYLNITROSAMINE, RAT (0956)
 DIMETHYLAMINOAZOBENZENE, HEPATOMA, RAT (2423)
 ENVELOPE-ANTIGEN RELATIONSHIPS, HAMSTER-SPECIFIC SARCOMA VIRUSES (0551)
 EPSTEIN-BARR, CLONED HUMAN LEUCOCYTES (1021)
 EPSTEIN-BARR, VIRUS ENVELOPE, LYMPHOID CELLS (0156)
 ERYTHROCYTE ISOANTIGEN, VIRUS SUSCEPTIBILITY, AVIAN LEUKOSIS-SARCOMA VIRUS (0160)
 FERRITIN, VIRUS PARTICLE, MAMMARY TUMOR, MOUSE (2347)
 FOCUS FORMATION, HUMAN SARCOMAS IN VITRO (1427)
 GASTRIC CANCER, EMBRYONAL TISSUE, NORMAL STOMACH, MAN (0707)
 GASTROINTESTINAL MALIGNANCIES, HUMAN FETAL GUT ANTIGEN (1566)
 ALPHA-2-GLOBULIN, CANCER PATIENTS URINE, IMMUNOELECTROPHORESIS (0731)
 GLYCOPROTEIN, MAMMARY TUMOR AGENT (0191)
 GROSS VIRUS, MURINE LEUKEMIA (1523)
 GROUP-SPECIFIC, AVIAN MYELOBLASTOSIS VIRUS (0582)
 GROUP-SPECIFIC, C-VIRUS, LEUKEMIA, RODENT (2457)
 GROUP-SPECIFIC, FELINE LEUKEMIA VIRUS (1975), (1977)
 GROUP-SPECIFIC, FELINE LEUKEMIA VIRUS, ISOLATION (2312)
 GROUP-SPECIFIC, IMMUNOLOGICAL IDENTITY REACTIONS, HAMSTER-SPECIFIC C-TYPE VIRUS (0552)
 GROUP-SPECIFIC, MURINE C-TYPE RNA VIRUS (0597)
 GROUP-SPECIFIC, MURINE LEUKEMIA VIRUS (0598)
 GROUP-SPECIFIC, MURINE SARCOMA VIRUS (1476)
 GROUP-SPECIFIC, RNA TUMOR VIRUS, VIRUS (0562)
 HEPATITIS-ASSOCIATED, FAMILIAL HEPATOMA (1712)*
 HEPATITIS-ASSOCIATED, HEPATOCELLULAR CARCINOMA (0723)
 HEPATOMA, DIMETHYLAMINOAZOBENZENE, DIETHYLAMINOAZOBENZENE (0434)
 HERPES SIMPLEX VIRUS, CERVICAL CARCINOMA (0623)
 HL-A, HODGKIN'S DISEASE, LEUCOCYTE PHENOTYPE (0717)
 HL-A, LEUKEMIC CELLS (0714)
 HUMAN WART (2017)
 IMMUNOFLUORESCENCE, ADENOVIRUS-ASSOCIATED VIRUS, HERPES VIRUS (0179)
 LEUCOCYTE, HODGKIN'S DISEASE (0718)
 LEUKEMIA, ASCITES TUMOR (1549)
 LEUKEMIA, COMPLEMENT BINDING (0711)
 LEUKEMIA, ISOLATION, MAN (1141)*
 LEUKEMIA, LYMPHOMA, THYMUS-LYMPHOID TISSUE (1121)
 LOW-LEUKEMIC STRAIN MICE, MURINE LEUKEMIC STRAIN MICE (0596)
 LYMPH NODE CELLS, DNA, PHYTOHEMAGGLUTININ (0238)
 LYMPHOBLASTOID CELLS, BURKITT'S LYMPHOMA, EPSTEIN BARR VIRUS (1532)
 LYMPHOCYTES, MALIGNANT LYMPHOMA (1542)
 MAMMARY TUMOR VIRUS, BLOOD, TISSUE, MICE (2349)
 MAREK'S DISEASE, HERPESVIRUS, PATHOGENICITY (1467)
 MELANOMA, ACUTE LEUKEMIA, HUMAN (1129)
 3-METHYLCHOLANTHRENE, MURINE SARCOMAS (0468)
 METHYLCHOLANTHRENE SARCOMA, TRANSPLANTATION, GUINEA PIG (1985)
 MILK ANTIGEN ASSAY, MOUSE MAMMARY TUMOR VIRUS, INOCULATION AGE (0194)
 MOUSE EMBRYO EXTRACT, CANCER TISSUE (0721)
 MURINE SARCOMA VIRUS (2458)
 NEUROBLASTOMA, FETUS, ADRENALS (1577)
 POLYPEPTIDE, AVIAN MYELOBLASTOSIS VIRUS (1065)
 PROTEIN SYNTHESIS, MYELOMA CELL-LYMPHOMA CELL HYBRID (1124)
 RESPONSE, DEFECTIVE VIRUS, SV40 (1100)
 ROUS SARCOMA VIRUS COAT, HETEROKARYOTIC CELLS (0201)
 S BLOOD, SS PHENOTYPE, BREAST CANCER (1130)

RCOMA, FERRIDEXTRAN SPOFA, RAT (0900)
 RCOMA, HUMAN ADENOVIRUS TYPE 12, GROWTH ENHANCEMENT, HAMSTER (1050)
 RCOMA, MIGRATION INHIBITION, MICE (2420)
 RCOMA 180, 15 VIRUSES (1995)
 NSITIZED MICE, SERUM PROTEIN CONCENTRATIONS, PRECANCEROUS CHANGES (1587)
 RUM, LYMPHOID TUMOR, CHICKEN (2439)
 RUM, MAMMARY CANCER, MURINE (2422)
 RUM, MYELOMA, PROTEINS (LAMBDA) (1127)
 EEP ERYTHROCYTES, HAMSTER CELLS, VIRUS, GLYCOPROTEINS (2437)
 OPE PAPILLOMA VIRUS (0658)
 ECIFICITY, CHEMICALLY-INDUCED TUMOR, VIRAL TUMORS, REVIEW (0361)
 ECIFICITY, INTRASPECIES, INTERSPECIES, C-TYPE VIRUSES (2407)
 ECIFICITY, 3-METHYLCHOLANTHRENE, DIFFERENTIAL ANTIGENICITY SARCOMAS (0942)
 LEEN, RETICULUM CELL SARCOMAS, AGE, MICE (2001)
 IMULATION, LYMPHOMA DEVELOPMENT, IMMUNOSUPPRESSIVE TREATMENT (1539)
 BUNITS, HEMAGGLUTINATION-INHIBITION ASSAY, RAUSCHER LEUKEMIA VIRUS (2409)
 LFANILIC ACID-CONJUGATED, OVARIAN ASCITES TUMOR, RAT (0732)
 RFACE, FRIEND VIRUS, RAT TUMOR (1533)
 RFACE, MYELOMA, CYTOTOXICITY, MOUSE (2415)
 RFACE, PROTEIN COMPONENTS, AVIAN TUMOR VIRUS (1085)
 RFACE AND TUMOR, VIRUS-SPECIFIED DNA, SIMIAN VIRUS 40 (0209)
 40, ADENOVIRUS, 2-SV40 HYBRIDS (1980)
 40, TRANSFORMED HAMSTER CELLS (1525)
 ADENOVIRUS-INDUCED TUMOR, FREEZING TREATMENT (0177)
 AMINO ACID COMPOSITION, ADENOVIRUS TYPE 12, HAMSTER (1526)
 ANSFORMED CELLS, SV40, UV-IRRADIATED (1537)
 ANSPLANTATION, ADENOVIRUS SA7, HAMSTER (0616)
 ANSPLANTATION, HUMAN, MOUSE LEUKEMIA VIRUS, ETIOLOGY, MONONUCLEOSIS (1738)
 ANSPLANTATION, SV40 (0670)
 ANSPLANTATION, TUMOR GLYCOPROTEINS, REVIEW (1758)*
 TA, ADENOVIRUS TYPE-12, MOUSE (1456)
 MOR, ANTI-TUMOR REACTIONS (1754)*
 MOR, CELL CLONES, POLYOMA VIRUS, MOUSE (2391)
 TUMOR, CELL TRANSFORMATION, SV40 (0349)
 TUMOR, FRIEND VIRUS, MODIFICATION (0170)
 TUMOR, INHIBITION OF MIGRATION, MACROPHAGE MIGRATION (1554)
 TUMOR, POLYOMA VIRUS, RAT (2454)
 TUMOR, SV40, KIDNEY CELLS (1538)
 TUMOR COMPLEMENT FIXING, POLYOMA VIRUS (1510)
 TUMOR-SPECIFIC, ALPHA-FETOGLOBULIN, DIGESTIVE TRACT CANCER (0362)
 TUMOR-SPECIFIC, RAT MAMMARY CARCINOMA, ISOLATION (1132)
 TUMOR-SPECIFIC ANTIGEN, ROUS SARCOMA VIRUS, MOUSE (0653)
 TUMOR-SPECIFIC NEOANTIGEN, VIRUS, HUMAN MAMMARY CARCINOMA (1131)
 TUMOR SPECIFIC TRANSPLANTATION, ADENO-VIRUS, VIRUS INDUCED TUMORS (0180)
 ULTRAVIOLET IRRADIATION, VIRUS (1978)
 VARIATION, IMMUNOCHEMICAL ANALYSIS, POLYOMA VIRUS (1107)
 VIRAL, HERPES, CELL MEMBRANES (1062)
 VIRAL, LOCALIZATION, IMMUNOFERRITIN, HERPES SIMPLEX (1521)
 VIRAL ANTIBODY, FELINE LEUKEMIA VIRUS (0163)
 VIRUS, EPSTEIN-BARR VIRUS, MAREK'S DISEASE HERPES VIRUS (1028)
 VIRUS, MOUSE, HAMSTER, CAT, C-TYPE (2356)
 "VIRUS FREE" TUMORS, ROUS SARCOMA VIRUS (0655)
 ANTIMETABOLITE
 ALKYLATING AGENTS, ANTIBIOTICS, CANCER CHEMOTHERAPY, CARCINOGENICITY, RAT (0906)
 ANUS
 CARCINOMA, PATHOGENESIS, HUMAN (1164)*
 AORTA
 SWINE, HYPERLIPEMIC DIET, UNDIFFERENTIATED SUBENDOTHELIAL CELLS (0261)
 APLASIA
 HEMATOLOGY, LEUKEMIA, BENZENE EXPOSURE, EPIDEMIOLOGY (0121)*
 AROMATIC AMINES
 GENETIC ACTIVITY, MITOTIC CONVERSION, YEAST CELLS (0412)
 AROMATIC HYDROCARBON
 CARCINOGENICITY, ELECTRON TRANSFER ENERGIES, HYDROPHOBIC PROTEIN BINDING (2153)
 CARCINOGENICITY IN WATER ENVIRONMENT, BENZO(A)PYRENE (0865)*
 HEMOPATHY, HUMANS, OCCUPATIONAL HAZARD (1370)
 INTERCALATION, POLYADENYLIC ACID (0410)
 MICROSOMES, CYTOCHROME PI-450, RAT (1344)
 PETROLEUM ASPHALTS, COAL-TAR PITCH, SKIN TUMORIGENESIS (1330)
 PHOTOCARCINOGENICITY, MECHANISM (0345)
 POLYCYCLIC, CARCINOGEN BINDING, DNA TEMPLATE (2266)*

ARSENIC

EPITHELIOMA, BOWEN'S DISEASE, HUMANS (1368)

ASBESTOS

BRONCHIAL CANCER, PLEURAL MESOTHELIOMA (1610)

DUST, LUNG GRANULOMAS, MICE, HAMSTERS (1852)

DUST EXPOSURE, PULMONARY FUNCTION, OCCUPATIONAL EXPOSURE (1857)

ENGLAND, PLEURAL MESOTHELIOMA (1858)

EXPOSURE, CLINICAL FEATURES, DIFFUSE PLEURAL MESOTHELIOMA (1004)

FERRITIN, MESOTHELIOMA, LUNG, ABDOMEN, HUMAN (2257)

MALIGNANT MESOTHELIOMA, MINING (0268)

NETHERLANDS SHIPYARDS, MESOTHELIOMA (2046)

OCCUPATIONAL EXPOSURE, MESOTHELIOMA, SCOTLAND (1170)

PLEURAL AND PULMONARY ASBESTOSIS, EARLY RADIOLOGICAL CHANGES (1263)*

ASCITES

ANTIGEN, LEUKEMIA (1549)

EHRlich, ANTIBODIES, COMPLEMENT, HUMAN SERUM (2417)

EHRlich TUMOR, LIVER ARGINASE, UREA CYCLE ENZYME (2067)

EHRlich TUMOR CELLS, UROPORPHYRIN (1702)

GUINEA PIG, MYCOBACTERIUM BOVIS, INHIBITION OF TUMOR GROWTH (0727)

3'-METHYL-4-DIMETHYLAMINOAZOBENZENE, HEPATOCARCINOMA, RAT (0429)

PERITONEAL FLUID, HEPATOMA, IMMUNITY (1555)

SARCOMA 180, MRNA, POLYSOME (2071)

TUMOR, DNA, ORTHOPHOSPHATE, THYMIDINE, LIVER (1648)

TUMOR, N-NITROSOBUTYLUREA, MYELOGENOUS GRANULOCYTIC LEUKEMIA (1353)

TUMOR, TRANSFER OF PROTEINS TO NUCLEOLUS, MOUSE (1658)

TUMOR CELLS, ADENINE NUCLEOTIDE, MICE (2065)

ASTROCYTOMA

DNA REPLICATION, HUMAN (1230)

N-NITROSOMETHYLUREA, GLIOBLASTOMA, RAT (1991)

N-NITROSOMETHYLUREA, GLIOMAS, RAT (1821)

ATOMIC BOMB

SMALL G CHROMOSOME, ABERRATIONS (0541)

ATP

ATPASE ACTIVITY, HEPATOMA, PLASMA MEMBRANE OF LIVER CELLS (0258)

NUCLEAR ATPASE LOCALIZATION, MOUSE HEPATOMA (0259)

AUTOIMMUNE DISEASE

LYMPHOPROLIFERATIVE CHANGE, GERM-FREE MICE (0168)

AXILLA

SARCOMA, 3,4-BENZOPYRENE, MOUSE (0467)

AZATHIOPRINE

CERVIX, DYSPLASIA, HUMAN (0692)

CHROMOSOMAL MUTATIONS, HUMAN LEUKOCYTES, OXIMAZON (1766)

AZIRIDINE ETHANOL

SARCOMA INDUCTION, PROPANE SULFONE (1291)

AZO DYE

HEPATOMA, ULTRASTRUCTURE, RAT (1785)

SYNTHESIS, RAT LIVER, 4-AMINO-2',3'-DIMETHYLAZOBENZENE (0432)

BACILLUS CALMETTE-GUERIN

INOCULATION OF BACILLUS, LEUKEMIA INCIDENCE (1250)

MAMMARY TUMOR ENHANCEMENT, 7,12-DIMETHYLBENZ(A)ANTHRACENE (1243)

METHYLCHOLANTHRENE, RATS, MICE, TUMOR TISSUE (2238)

3-METHYLCHOLANTHRENE, CARCINOGENESIS IN MOUSE (2272)*

MYCOBACTERIUM BOVIS, FRIEND DISEASE VIRUS, IMMUNITY (1903)

VACCINATION, SCOTLAND, LEUKEMIA MORTALITY (1251)

BACTERIA

MALIGNANCY, BACTERIAL CARCINOGENESIS (1726)

MUTANTS, 4-NITROQUINOLINE-1-OXIDE, BACTERIOPHAGE (0489)

ROUS SARCOMA VIRUS (1946)

TUMORS, LEUKEMIA (2124)

BACTERIOPHAGE

TRANSFER RNA, E. COLI (2513)

BENZ(C)ACRIDINES

DNA, DIMETHYL DERIVATIVES, INTERACTION (2178)

BENZENE

CHROMOSOME DAMAGE, BONE MARROW (0030)

GRANULOCYTIC LEUKEMIA, CHROMOSOME STUDY (2273)*

LEUKEMIA, EPIDEMIOLOGY (0121)*

OCCUPATIONAL EXPOSURE, LEUKEMIA INCIDENCE, ATOMIC BOMB IRRADIATION (1399)

SINUS LYMPHOCYTES, FOLLICULAR LYMPHOCYTES, HEMOGRAMS (0983)

TOLUENE, OCCUPATIONAL HAZARD, ALKALINE PHOSPHATASE, LEUKOCYTE LEVELS (1374)*

TOLUENE, OCCUPATIONAL HAZARD, CHROMOSOME CHANGES (2193)

BENZENE HEXACHLORIDE

ACUTE LEUKEMIA, OCCUPATIONAL EXPOSURE (0509)

BENZIDINE

TRYPTOPHAN METABOLISM, 3-HYDROXY-ANTHRANILIC ACID, RAT (0911)

8,9-BENZO-GAMMA-CARBOLINE

STRUCTURE-CARCINOGENICITY RELATIONSHIPS, MOUSE (0411)

BENZO(A)PYRENE

AIRPLANE ENGINE SOOT, MOUSE (2228)

ANTIMITOTIC EFFECT, CELL CULTURES, LUNG, RAT (0460)

3,4-BENZFLUORANTHENE, CARCINOMATOUS TISSUE, STOMACH, RECTUM (0912)

BROILED OIL, CARCINOGENICITY, RAT (2196)

CARCINOGENICITY IN WATER ENVIRONMENT

POLYNUCLEAR AROMATIC HYDROCARBONS

COCARCINOGEN, TOBACCO, SKIN, MOUSE
 (2204)
 FIBROSARCOMA, CYCLOPHOSPHAMIDE,
 HYDROCORTISONE, RAT LIVER (1815)
 FIBROSARCOMA, EMBRYO, HAMSTER (1331)
 FIBROSARCOMA, IMMUNOREACTIVITY, RNA
 (0222)
 FIBROSARCOMA, 3-METHYLCHOLANTHRENE,
 PROSIMIANS (0073)
 FIBROSARCOMA TUMOR CELL INOCULA,
 RETARDATION OF PRIMARY TUMOR GROWTH
 (0940)
 HUMAN ORGANS, AGE, CARCINOGEN (1333)
 HYDROXYLASE, FLAVONE, PULMONARY
 ADENOMA (0070)
 HYDROXYLASE, LUNG, HAMSTER (2230)
 HYDROXYLATION, HUMAN PLACENTA,
 TOBACCO (1799)
 HYDROXYLATION, INHIBITION KINETICS
 (0069)
 LARYNGEAL CANCER, OCCUPATIONAL EXPO-
 SURE (0117)*
 LUNG, RATS, METABOLISM, ELIMINATION
 (0936)
 LUNG, UPTAKE, HAMSTER (2229)
 LUNG TUMORS, SILICOTIC DUSTS, RAT
 (0122)*
 METABOLISM, CARBON MONOXIDE, LIVER,
 RAT (0459)
 METABOLISM, COLD-BLOODED VERTEBRATES,
 WARM-BLOODED VERTEBRATES (0937)
 METABOLISM, MACROMOLECULE BINDING
 (0941)
 METABOLISM OF CARCINOGEN, CIGARETTE
 SMOKE (1796)
 METABOLISM OF CARCINOGEN, PRETREATMENT
 WITH HYDROCARBONS (1335)
 METABOLITES IN RAT BILE (1334)
 MICROSOMAL DRUG-METABOLIZING ENZYMES,
 BILIARY EXCRETION (0458)
 MICROSOMAL HYDROXYLASE, AFLATOXIN B1
 INHIBITION (0428)
 MOUSE TUMOR, IMMUNOBLOBULIN IGG2
 (1133)
 OCCUPATIONAL EXPOSURE, COKE OVEN
 (1800)
 OCCUPATIONAL HAZARD, ALUMINIUM PLANT
 (2259)
 OCCURRENCE, SYNTHESIS, MAN, ANIMAL
 (1747)
 POLLUTION, FIBROSARCOMA, MOUSE (2258)
 PREGNANT MICE, PULMONARY ADENOMAS IN
 PROGENY (1332)
 PYRENE, TRANSPLACENTAL ACTION, KIDNEY
 TISSUE, MOUSE (2231)
 RAT ETHANOL METABOLISM (0119)*
 RNA, IMMUNITY, SARCOMA, RAT (2428)
 RNA FROM TUMOR-IMMUNE ANIMALS, TUMOR
 IMMUNITY TRANSFER (0728)
 SARCOMA, AXILLARY REGION, MOUSE (0467)
 SKIN, NEUTRAL FRACTION, CIGARETTE
 SMOKE, MICE (1798)
 SMOKED FISH, JAPAN, DIET (2202)
 TUMOR, LUNG, SKIN, MOUSE FETUS
 (1797)
 UV RADIATION, DNA, PHOTO ADDUCT (0938)
 WATER POLLUTION INDEX, WATER ORGAN-
 ISMS, U.S.S.R. (0515)*

WATER SOLUBILITY, EFFECT OF CAFFEINE
 (0989)*
 P-BENZOQUINONE
 INHALATION, MOUSE BRONCHIAL CELLS,
 MALIGNANT CHANGES (1336)
 BENZO(B)THIOPHENE
 DERIVATIVES, CARCINOGENICITY (0863)*
 BERYLLIUM
 CHRONIC INTOXICATION, OCCUPATIONAL
 EXPOSURE, CANCER (0981)
 EXPOSURE, LUNG CANCER (0300)*
 BETEL-NUT
 BUCCAL MUCOSA, TOBACCO CHEWING (0978)
 CHEWING, TOBACCO CHEWING, HISTOLOGY
 OF BUCCAL MUCOSA (0979)
 BILE DUCT
 CANCER, CHRONIC ULCERATIVE COLITIS
 (1708)*
 CARCINOMA, ULCERATIVE COLITIS (1249)
 GENETIC SUSCEPTIBILITY, SPONTANEOUS
 CHOLANGIOMA, MICE (1695)
 HEPATOBILIARY TRACT, TUMOR, INCIDENCE,
 SOUTHERN ITALY (1630)*
 BIS(CHLOROMETHYL) ETHER
 CHRONIC INHALATION, LUNG ADENOMAS,
 MICE (1761)
 BLADDER
 2-ACETYLAMINOFLUORENE, 4-ETHYL-
 SULFONYLNAPHTHALENE-1-SULFONAMIDE,
 MOUSE, EPITHELIUM (1300)
 CANCER, LOWER URINARY TRACT CANCER,
 CIGARETTE SMOKING (0976)
 CANCER, SEX DIFFERENCE IN INCIDENCE,
 CIGARETTE SMOKING (0511)
 CARCINOMA, BETA-AMINOISOBUTYRIC ACID
 (0336)*
 CARCINOMA, ESTABLISHED CELL LINES,
 EPITHELIAL, N-2-FLUORENYLACETAMIDE
 (1304)
 CARCINOMA, LABORATORY WORKER, CHEMICAL
 CARCINOGEN (0367)
 CARCINOMA, LYMPHOCYTE INFILTRATION (1579)
 CARCINOMA, PATHOLOGY, EPIDEMIOLOGY,
 REVIEW (0380)*
 CARCINOMA, SCHISTOSOMIASIS (0369)
 DIBUTYLNITROSAMINE, TUMOR, MOUSE
 (0481)
 EPITHELIAL TUMOR, DARK CELLS,
 HISTOCHEMISTRY, HUMANS (2028)
 N-2-FLUORENYLACETAMIDE DIET, CYCLO-
 PHOSPHAMIDE (1302)
 PAPILLOMA, 2-NITRONAPHTHALENE, MONKEY
 (0027)
 RAT TUMOR, RESTRICTION OF PUBLIC
 CONSUMPTION, CYCLAMATES (0420)
 S. HAEMATOBIIUM, CARCINOMA (0771)
 TRANSITIONAL CELL TUMOR, CHROMOSOME
 PATTERN, HUMAN (2099)
 TUMORS, 2-ACETYLAMINOFLUORENE,
 DIETARY INDOLE (0907)
 TUMORS, DIETARY BRACKEN FERN, THIAMINE
 (0899)
 TUMORS, DNA, B-GLUCURONIDASE, HUMAN
 (2084)
 TUMORS, TEXTILE WORKERS, HIGH-RISK
 OCCUPATIONS (0980)
 URINARY, DIBUTYLNITROSAMINE TUMORS,
 RAT (2024)

URINARY, SQUAMOUS METAPLASIA, GIANT VESICAL CALCULUS (2140)*
WALL, 3-METHYLCHOLANTHRENE, SPECTROPHOTOMETRY, RAT (0948)

BLOOD
CYTOMETRIC STUDY, IRRADIATED BONE MARROW LYMPHOCYTES, SPLENIC LYMPHOCYTES (0534)
GROUPS, TUMOR INCIDENCE, PHENOTYPE, REVIEW (1284)*
HUMAN CELL CULTURES, ULTRASOUND EXPOSURE, CHROMOSOMAL ABERRATIONS (0527)
MALIGNANCIES, LIVER CARCINOMA, MYCOTOXINS (1276)
NEOPLASMS, METASTASES, MODEL (1681)
PERIPHERAL, BONE MARROW CELL, LEUKEMIA, HUMAN (0779)
PERIPHERAL BLOOD SMEARS, MALIGNANCY RELATED CYTOLOGIC CHANGES (0340)*
RETINOBLASTOMA, MALIGNANT CELLS (1666)
RH NEGATIVITY, LEUKEMIA, AGE DEPENDENT VARIATION (0801)
VESSELS, PLASMINOGEN, GRANULOMAS (2476)

BONE
CANCER, GROWTH PEAK, PUBERTY (0314)
CANCER, RADIUM EXPOSURE, CHILDREN (1000)
EPIDEMIOLOGY, MYELOMA (0266)
LESIONS, MURINE PLASMACYTOMAS, METASTASES (2143)*
MARROW CELL, PERIPHERAL BLOOD, LEUKEMIA, HUMAN (0779)
MARROW CELL COUNTS, X-IRRADIATION, METHIONINE SULPHOXIMINE (0405)
MARROW TRANSPLANTATION, RADIATION INJURY, SPLENECTOMY (0533)
OSTEOBLASTIC SARCOMA, OSSIFYING FIBROMA, MICE, ALKALINE PHOSPHATASE (1382)
OSTEOGENIC SARCOMA, EPIDEMIOLOGY, PATHOLOGY (0752)
OSTEOGENIC SARCOMA, IRRADIATION, MANDIBULAR FIBROUS DYSPLASIA (1408)*
OSTEOSARCOMA, STRONTIUM 90, RAT (1410)*
OSTEOSARCOMA, 32 PHOSPHORUS, ULTRASTRUCTURE (0548)
OSTEOSARCOMA, TIBIAL ENCHONDROMA (1707)*
PLUTONIUM, RETENTION (1012)
RADIUM KINETICS, THOROTRAST, MODEL, RABBIT (1403)*
RAPID GROWTH, ADOLESCENCE, ACUTE MYELOID LEUKEMIA (0375)
RNA, SARCOMA GROWTH, RAT (0817)
SKELETAL NEOPLASMS, ALKALINE PHOSPHATASE ACTIVITY (0327)
THORIUM 232, HUMAN (1006)
TRAUMA, WHOLE BODY IRRADIATION, OSTEOGENIC SARCOMA, MOUSE (1863)*
TUMORS, FBV VIRUS (0561)
TUMORS, MOLONEY MURINE SARCOMA VIRUS, HARVEY MURINE SARCOMA VIRUS (1938)
239PU EXPOSURE, SPECULATIVE ESTIMATE OF HAZARD, TUMOR RISK (1003)

XENOGENIC TRANSPLANT, OSTEOGENIC TRANSFORMATION, FIBROBLASTS (0738)

BONE MARROW
CELL COLONY, MONONUCLEAR CELL, GRANULOCYTE, STIMULATING SUBSTANCE (032)
CHLORAMBUCIL, BUSULPHAN (2070)
CHLORAMBUCIL, PROLIFERATION, SERUM, RAT (0901)
CHROMOSOME DAMAGE, BENZENE (0030)
COLONY-STIMULATING FACTOR, FACTOR SERUM TITER, RENAL INFLUENCE ON SERUM TITER, MOUSE (0332)
7,12-DIMETHYLBENZ(A)ANTHRACENE, RADIATION LEUKEMOGENESIS (0928)
DNASE, MICE, LEUKEMIA, VIRUS (1041)
FACTOR, THYMIC DNA SYNTHESIS STIMULATORY FACTOR (1657)
HEMATOPOIESIS, THYMUS, SPLEEN, RADIUM STRONTIUM (1379)
HUMAN MYELOMONOCYTIC LEUKEMIA, MICROCHROMOSOMES (1147)
HYDROGEN TRANSPORT, LEUKEMIA, HUMAN (2060)
IMMUNOFLOUORESCENCE MICROSCOPY, ACUTE LEUKOSIS, ACUTE MYELOSIS, CHILDREN (0233)
IONIZING RADIATION, HUMAN (0993)
OSTEOSARCOMA, STRONTIUM -90 (1381)
PROLIFERATION, LEUKEMIA (2170)*
RECONSTITUTION, X-IRRADIATION, IMMUNOLOGIC COMPETENCE, MICE (159)
STEM CELL PROLIFERATION, X-IRRADIATION (1011)
X-IRRADIATION, MITOTIC ABERRATIONS, RAT (1844)

BRACKEN FERN
DIET, DEVELOPMENT OF BLADDER TUMOR, THIAMINE (0899)

BRAIN
BLOOD BARRIER, TUMORS, METHYLNITROSOUREA, RAT (1822)
CEREBELLUM, 7,12-DIMETHYLBENZ(A)ANTHRACENE, TUMOR MODEL, RAT (222)
FIBROSARCOMAS, MONSTROCELLULAR SARCOMAS, METHYLCHOLANTHRENE (134)
HYPOPHYSIS, MORPHOLOGY, TUMOR, RAT (2580)*
HYPOTHALAMUS, MAMMARY GLAND, TUMOR, MOUSE (2501)
LESIONS, HISTOPATHOLOGY, PROTON-IRRADIATION (1007)
LIVER, MAMMARY TUMOR VIRUS, GR MOUS (0629)
MALIGNANCIES, ACID AND ALKALINE NUCLEASE (2080)
MALIGNANT INFILTRATION, CELLULAR BL NEVUS (1698)
MENINGIOMA, HYPERDIPLOIDY, CHROMOSOMES, HUMAN (1692)
MESENCHYMAL TUMORS, ORGAN TRANSPLANT PATIENTS (2138)
TRANSFER RNA, BASE COMPOSITION (252)
TUMOR, GROWTH BEHAVIOR, MATRIX CULTURE, HUMAN (0303)*
TUMOR, METHYLNITROSOUREA, RAT (0963)
TUMOR, TRANSPLACENTAL, ETHYLNITROSOUREA (0964)
TUMOR, TRNA, METHYLASE (2523)

TUMOR, TRNA, RRNA (2087)
 TUMOR ETIOLOGY, HORMONES, REVIEW
 (0844)
 TUMOR INFILTRATION, MYELIN BREAKDOWN,
 EHRLICH ASCITES TRANSPLANT, MOUSE
 (0253)
 BROMODEOXYURIDINE
 AVIAN SARCOMA VIRUS, VISIBLE LIGHT,
 CHICK EMBRYO FIBROBLAST (0641)
 ROUS SARCOMA VIRUS, RNA SYNTHESIS
 (0645)
 TRANSFORMED MOUSE KIDNEY CELLS,
 MITOMYCIN C, GENETIC CHANGE (0664)
 BROMO-ALPHA-ERGOCRYPTINE
 ERGOCORNINE, MAMMARY HYPERPLASTIC
 NODULE (1207)
 MAMMARY CARCINOMA, ENDOCRINE FUNCTION
 (0930)
 BROMOMETHYLBENZ(A)ANTHRACENE
 CARCINOGENICITY (0933)
 BROMOMETHYL-12-METHYLBENZ(A)ANTHRACENE
 CARCINOGENICITY (0933)
 RKITTS LYMPHOMA
 ANTIBODIES, EPSTEIN-BARR VIRUS (1973)
 AUTOIMMUNE SYSTEM, MALARIA, EPSTEIN
 BARR VIRUS (0005)
 CELL CULTURES, MITOTIC INDEX,
 PHYTOHEMAGGLUTININ (0730)
 CHILDREN, TUMORS OF HEAD AND NECK
 (1188)
 CYCLOPHOSPHAMIDE, CHROMOSOMAL ABERRA-
 TION (1364)
 EPSTEIN-BARR VIRUS (1432), (1886)
 EPSTEIN-BARR VIRUS, INFECTIOUS
 MONONUCLEOSIS (0154)
 EPSTEIN-BARR VIRUS, NASOPHARYNGEAL,
 CARCINOMA (1024)
 EPSTEIN-BARR VIRUS, NASOPHARYNGEAL
 CARCINOMA, DNA (0574)
 EPSTEIN-BARR VIRUS, TUMOR MEMBRANE
 ANTIGENS (1739)
 FEMALE TUMOR KARYOTYPE (1697)
 FOREIGN CELL CONTAMINATION (2305)
 HERPES SIMPLEX VIRUS, GROWTH (1923)
 IMMUNOSUPPRESSION, VIRUS (0687)*
 HERPES-LIKE VIRUS PARTICLES, ANTIGEN,
 MAN (2343)
 IMMUNOGLOBULINS, ISOANTIGENS, HUMAN
 (2158)
 INFECTIOUS MONONUCLEOSIS, LEUKEMIA,
 CELL POPULATION (2494)
 INHIBITION, HERPESVIRUS HOMINIS, VIRUS
 (2306)
 IODODEOXYPRIDINE, CYTOSINE ARABINOSIDE
 (1971)
 ITALIAN CASE (1699)
 LYMPHOBLASTOID CELLS, COMPLEMENT-
 FIXING ANTIGENS, EPSTEIN-BARR VIRUS
 (1532)
 LYMPHOSARCOMA, MALARIA (0689)*
 MALARIAL PARASITE, COCARCINOGEN (0690)*
 MEMBRANE ANTIGEN, EPSTEIN-BARR VIRUS,
 NASOPHARYNGEAL CARCINOMA (0578)
 MORPHOLOGY, EPSTEIN-BARR VIRUS (0575)
 NASOPHARYNGEAL CARCINOMA, ANTIBODY
 (0151)
 NASOPHARYNGEAL CARCINOMA, HERPES-TYPE
 VIRUS (1922)
 NEOCARZINOSTATIN, EPSTEIN-BARR VIRUS,
 VIRUS (1020)
 SERUM ANTIBODY, NASOPHARYNGEAL CAR-
 CINOMA SERUM ANTIBODY, EPSTEIN-BARR
 VIRUS (0153)
 URINE AND SERUM IMMUNOGLOBULINS (0573)
 VIRAL DNA DENSITIES, LUCKE ADENO-
 CARCINOMA FROG HERPESVIRUS, VIRUS,
 (0621)
 VIRUS, EPSTEIN-BARR VIRUS, VIRAL DNA
 (0688)*
 VIRUS, INCIDENCE, REVIEW (0870)*
 BURSA
 BURSAL LYMPHOID SYSTEM, MAREK'S
 DISEASE, HERPESVIRUS, BURSECTOMY
 (0162)
 BURSECTOMY, X-IRRADIATION, SPLEEN
 IMMUNE RESPONSE (1134)
 T-BUTYL HYDROPEROXIDE
 4-QUINOLINE-1-OXIDE, FREE RADICAL,
 SQUAMOUS CELL CARCINOMA, MICE (0026)
 CADMIUM
 CHLORIDE, SUBCUTANEOUS SARCOMA, RAT
 (0898)
 CAFFEINE
 BENZO(A)PYRENE, WATER SOLUBILITY
 (0989)*
 CALCIFICATION
 BREAST CANCER, FAT TRANSPLANTATION,
 HUMAN (1010)
 CALCIUM
 PROTEIN-BOUND, LYMPHOSARCOMA, EHRLICH
 CARCINOMA (1233)
 CANAVANINE
 ADENOVIRUS, INHIBITION OF REPLICATION
 (1046)
 CANCER
 ALL SITES, MORTALITY RATES, MORBIDITY
 RATES (0279)
 CHLORNAPHAZINE, HODGKIN'S DISEASE
 (0110)
 DETECTION, PHYSICAL EXAMINATION,
 EARLY SCREENING (0295)*
 DISSEMINATED MALIGNANT DISEASES,
 LEUCINE AMINOPEPTIDASE ACTIVITY
 (0788)
 ENDOMETRIUM, YOUNG WOMEN, PATHOGENESIS
 (0747)*
 EPIDEMIOLOGY, KURGAN (0754)
 EPIDEMIOLOGY, QUEBEC (0767)*
 ETIOLOGY, HORMONAL DISORDERS, REVIEW
 (0385)*
 MULTIPLE MALIGNANCIES, LOCALIZATION,
 ETIOLOGY (0772)
 CAPSID
 ADENOVIRUS TYPE 3,9,4,6, COCULTIVATION
 (2397)*
 PROTEINS, ADENOVIRUS (1043)
 CARBOHYDRATE
 METABOLISM, ADENOVIRUS TYPE-12, RAT
 (2333)
 METABOLISM, CHICK LIVER, AFLATOXIN B1
 (1311)
 REPRESSION, 3-METHYLCHOLANTHRENE,
 DIMETHYLNITROSOAMINE DEMETHYLASE (0474)
 CARBON TETRACHLORIDE
 HEPATIC LESIONS, 3-METHYLCHOLANTHRENE
 (0945)

HEPATOCARCINOGENESIS, CREATIVE KINASE,
MOUSE (1288)
CARCINOGENESIS
EXPERIMENT DESIGN, CHOLESTEROL, SODIUM
CYCLAMATE (0512)*
MECHANISM, PROTEIN MODIFICATION
KINETICS, CARCINOGENIC FACTORS
(1162)
MODEL, MALIGNANT TRANSFORMATION
IN VITRO, PHASES OF CELL GROWTH
(0854)
THEORY, CONTACT INHIBITION, CELL
PROLIFERATION (1728)
YTTERBIUM, GADOLINIUM (0403)
CARCINOGENICITY
AFLATOXIN B1, STRUCTURE-ACTIVITY
RELATIONSHIP (1308)
7-BROMOMETHYLBENZ(A)ANTHRACENE,
7-BROMOMETHYL-12-METHYLBENZ(A)
ANTHRACENE (0933)
DIBENZACRIDINES, STRUCTURE-ACTIVITY
RELATIONSHIP, SUPERDISLOCABILITY
INDEX, CHEMICAL DISPLACEMENTS
(0520)*
P-DIMETHYLAMINOAZOBENZENE,
N,N'-DIMETHYL-P-PHENYLAZOANILINE,
ELECTRON DENSITY STUDIES (0029)
ENHANCED DETECTION, TRANSPLACENTAL
EFFECTS, URETHANE, MOUSE (0972)
FOOD, ADDITIVES, REVIEW (2176)*
GERM-FREE STATE, TUMOR PROTECTION,
7,12-DIMETHYLBENZ(A)ANTHRACENE
(0065)
HUMAN MALIGNANCY, E16 CHROMOSOME
(2095)
MECHANISM, AFLATOXIN, NUCLEIC ACID
SYNTHESIS (0049)
MECHANISM, ALKYLNITROSAMINES, ELEC-
TRONIC STRUCTURES (0472)
4-NITROQUINOLINE-1-OXIDE, REVIEW
(1746)
8-OXYQUINOLINE, MOUSE, RAT (0487)
PHENANTHRENE, DIBENZ(A,H)ANTHRACENE,
K-REGION EPOXIDE (0067)
POLYPHENOLS, TOBACCO, MOSAIC VIRUS
(1836)*
SEVIN, MANEB, CIRAM, CINEB, RAT
(1290)
TOBACCO CONDENSATES, ESTERASE ACTIVITY
AREA TEST (0499)
CARCINOMA
ACHALASIA, ESOPHAGUS (1700)
ADRENAL, HUMAN, STEROID ANALYSIS
(0782)
ANAL FISTULA, PATHOGENESIS (1164)*
ANO-RECTAL FISTULA, PATHOGENESIS, MAN
(0341)*
BASAL CELL, BURN SCARS, RADIATION
THERAPY (0531)
BLADDER, SCHISTOSOMIASIS (0369)
BRONCHOGENIC CARCINOMA, HISTOPATHOLOGY
HUMAN (0764)
CAUSTIC ULCERATION, ESOPHAGUS, BOUGIE
(0988)*
CERVICAL SQUAMOUS CELL, POSTMENOPAUSAL
WOMEN (0313)
CIGARETTE TAR, LYMPHOMA, NEWBORN ICR
MICE (0105)

9,10-DIMETHYL-1,2-BENZANTHRACENE,
IRRADIATION, PROLIFERATION KINETICS
(0068)
EPIDERMAL, RESPIRATORY TRACT,
N-NITROSO-N-METHYLUREA, HAMSTER
(0482)
ERLICH SUBCUTANEOUS, 5-N-METHYLATED
LYSINE, GROWTH-PROMOTING EFFECTS (081)
GASTRIC, GERMANY, DETECTION, MORTALITY
(0765)
LEUKEMIA, COMBINED CASES (2578)*
LIVER, RAT, N-HYDROXY-N-2-FLUORENYL-
ACETAMIDE (0409)
MAMMARY GLAND, OTHER BREAST, REVIEW
(0014)
MAMMARY GLAND, RAT, 9,10-DIMETHYL-1,2-
BENZANTHRACENE (0442)
MODEL, LUNG CELLS, CHINESE HAMSTER
(1675)
NASOPHARYNGEAL, EPSTEIN-BARR VIRUS,
SURFACE ANTIGEN (0579)
NASOPHARYNGEAL CARCINOMA, BURKITT'S
LYMPHOMA, EPSTEIN-BARR VIRUS, DNA
(0574)
NASOPHARYNX, SIBLINGS (0316)
PENIS, PAINT, PAINT REMOVERS (0114)
POLYP, LARGE INTESTINE, CHROMOSOME
(0325)
SCROTUM, INDUSTRIAL HYGIENE, OCCUPA-
TIONAL FACTORS (0116)
SQUAMOUS CELL, DESMOSOMES, KERATINO-
CYTES, HUMAN (1231)
SQUAMOUS CELL, SUBMUCOUS FIBROSIS,
PRECANCEROUS CONDITION (0247)
STOMACH, RECTUM, BENZO(A)PYRENE,
3,4-BENZFLUORANTHENE (0912)
SUPERFICIAL BASAL CELL, TUMOR BUD CELL
MORPHOLOGY (0735)
CAROTID BODY
TUMORS, FAMILIAL OCCURRENCE, BILATERAL
TUMOR (1258)
CARRAGEENAN
GRANULOMA, FREUND'S ADJUVANT (0103)
CARTILAGE
XIPHISTERNAL, EPITHELIOMA, INVASION
(0250)
CASTRATION
ESTRADIOL, THYROID, EPIDERMAL CYST,
RAT (0416)
CELL
AKR-A CULTURE, LYMPHOID LEUKEMIA,
GROSS LEUKEMIA VIRUS, MOUSE (0171)
BHK 21 HAMSTER, DNA SYNTHESIS, POLYOMA
VIRUS, SERUM (0216)
CARCINOGENIC, HYBRIDIZATION, HAMSTER
(1715)*
CHICK EMBRYO, INTERFERON INDUCTION,
VIRUS, ADENOVIRUS (0178)
CHICK EMBRYO, ROUS SARCOMA VIRUS,
SUGAR TRANSPORT (0204)
CULTURE, 3,4-BENZANTHRACENE, ANTI-
MITOTIC EFFECT, LUNG, RAT (0460)
CULTURE, MITOTIC RATE, MOLONEY VIRUS,
ANTIGEN (1473)
CULTURE, MURINE SARCOMA VIRUS, MURINE
LEUKEMIA VIRUS (0199)
CYCLE, AUTORADIOGRAPHIC ANALYSIS,
SOLID HUMAN TUMORS (0302)*

CYCLE, ULTRAVIOLET IRRADIATION, MURINE SARCOMA VIRUS INFECTION (0198)
 DARK, URINE BLADDER TUMOR, HUMANS (2028)
 DIFFERENTIATION, MURINE PLASMOCYTOMA, IN VITRO (0819)
 EMBRYONIC, NEOPLASTIC, MINIMUM DEVIATION (0293)
 EMBRYONIC CULTURE, RAUSCHER MURINE LEUKEMIA VIRUS, TYPE-C VIRUS PARTICLE (0175)
 EPENDYMOMA, MORPHOLOGY, HUMAN (0249)
 EPIDERMAL, NEUTRON IRRADIATION, MOUSE (1409)*
 EPITHELIAL CELLS, URINARY BLADDER CARCINOMA, N-2-FLUORENYLACETAMIDE (1304)
 FIBROBLAST, OSTEOGENIC TRANSFORMATION, XENOGENIC BONE TRANSPLANTS (0738)
 FUSION, POLYKARYOCYTOSIS, VIRUS (1019)
 FUSION, VIRUS, MURINE LEUKEMIA (2315)
 GROWTH, DIFFERENTIATION, HETEROTOPIA, MALIGNANCY (0379)*
 HAMSTER EMBRYONIC, KARYOTYPE CHANGES, 4-NITROQUINOLINE-1-OXIDE (0098)
 HETEROKARYOTIC CELLS, VIROGENIC CELL FUSION, ROUS SARCOMA VIRUS COAT ANTIGEN (0201)
 HYBRIDS, SV40 PRODUCTION, UV RADIATION IN VITRO (1517)*
 LEUKEMIA, IMMUNOLOGY, HUMAN (2406)
 LEUKEMIC MOUSE CELL LINE, MURINE MYELOPROLIFERATIVE VIRUS (0166)
 LEYDIG CELL TUMOR, DIETHYLSTILBESTROL, DNA SYNTHESIS (0022)
 LYMPH NODE, DNA, PHYTOHEMAGGLUTININ, ANTIGEN (0238)
 LYMPHOBLASTIC TRANSFORMATION, PHYTOHEMAGGLUTININ INDUCED, IN VITRO, MAN (0242)*
 LYMPHOCYTE, DEDIFFERENTIATION, PHYTOHEMAGGLUTININ INDUCED, MAN (0243)*
 LYMPHOCYTE, STIMULATION, ANTIGEN, MELANOMA (0230)
 LYMPHOCYTE TRANSFORMATION, AFLATOXIN B, PHYTOHEMAGGLUTININ (0045)
 MYOEPITHELIAL, ROLE IN BENIGN AND MALIGNANT TUMORS (2035)*
 NEOPLASTIC MAST CELL, PHOSPHOLIPID TURNOVER (0256)
 NEW LINES, CANCER VIRUS, SV40, KIDNEY, HUMAN SERUM (1501)
 PLASMA CELL TUMOR, FREUND ADJUVANT, CHROMOSOMAL ALTERATION (0102)
 POLYOMA-TRANSFORMED, GROWTH REGULATION MOUSE, HAMSTER (0350)
 POPULATION KINETICS, CAPILLARY ENDOTHELIAL CELLS, MOUSE MAMMARY TUMOR (0762)
 PROLIFERATION, POLYOMA VIRUS, MURINE (2389)
 RECOGNITION SITE, PROLIFERATION, CONTROL, LYMPHOCYTE (0008)
 RESPONSE, ROUS SARCOMA VIRUS, SMALLPOX VACCINE VIRUS, VESICULAR STOMATITIS VIRUS (0560)
 SENSITIVITY TO VIRAL INFECTION, MOLONEY LEUKEMIA VIRUS, JLSV-9 CELLS (1445)

SPLEEN, LYMPHOMA, MICE (0224)
 SURFACE ELECTRIC POTENTIAL, MALIGNANT CELL (0252)
 SURFACE PROPERTIES, OCULAR MELANOMA, ULTRASTRUCTURE (1670)
 SUSPENSION, SURFACE INTERACTIONS, POLYOMA VIRUS (2387)
 SYNGENIC LIVER, METHYLCHOLANTHRENE, TUMOR INHIBITION (0079)
 TRANSFORMATION, ONCOGENIC RNA VIRUS, REVIEW (0020)*
 TRANSFORMATION, POLYOMA VIRUS, VIRUS GENERATION IN VITRO (0667)
 TRANSFORMATION STAGES, ROUS AND POLYOMA VIRUS INDUCED, HAMSTER (0556)
 TRANSFORMED, SURFACE MEMBRANE, CARBOHYDRATE (0708)
 YOSHIDA SARCOMA, 4-NITROQUINOLINE-1-OXIDE, CHROMOSOME ABERRATION, PERSISTENT NUCLEOLI (0097)
 CENTRAL NERVOUS SYSTEM
 INTRACRANIAL MENINGEOMA, FAMILIAL, HUMAN (1262)
 TUMORS, BLOOD BRAIN BARRIER, METHYLNITROSOUREA, RAT (1822)
 CERVIX
 ATYPIA, PREVALENCE AND INCIDENCE, COMPUTERIZED STUDY (2045)
 CANCER, CERVICAL DYSPLASIA, ORAL CONTRACEPTIVE (0281)
 CANCER, ENDOMETRIAL CANCER, ISRAELI POPULATION (1175)
 CANCER, EPIDEMIOLOGY, EARLY DETECTION, CANADA, REVIEW (0368)
 CANCER, MULTIPLE TUMORS, THERAPY (2137)
 CANCER, RISK IN PAROUS INDIAN WOMEN, EPIDEMIOLOGY (2042)
 CANCER, TRICHOMONAS VAGINALIS (1265)*
 CANCER MORTALITY, CYTOLOGIC SCREENING (0297)*
 CARCINOMA, ANTIBODIES, HERPESVIRUS TYPE 2 (1924)
 CARCINOMA, CHROMOSOME CHANGES (0809)
 CARCINOMA, FIBROBLASTS, SKIN (1562)
 CARCINOMA, HERPESVIRUS ANTIGENS, HERPES SIMPLEX VIRUS (0623)
 CARCINOMA, KIDNEY TRANSPLANT, IMMUNOSUPPRESSION (1582)*
 CARCINOMA, MUCOSUBSTANCE, HUMAN (2109)
 CARCINOMA, RECTUM, RADIATION THERAPY (1395)
 CARCINOMA, SEQUENTIAL ORAL CONTRACEPTIVE, CYTOLOGIC ABNORMALITIES (0504)
 CARCINOMA, TEEN-AGE PATIENTS, CYTOLOGIC ATYPIA (0744)
 CERVICAL NEOPLASTIC CHANGE, RESERVE CELL HYPERPLASIA, INCOMPLETE SQUAMOUS METAPLASIA (1585)
 CERVICO-VAGINAL TUMORS, 7,12-DIMETHYLBENZ(A)ANTHRACENE, L-THYROXINE, METHYLTHIOURACIL, RATS (0887)
 CHROMOSOME, ADENOCARCINOMA (0254)
 CONE BIOPSY, EARLY CERVICAL CANCER (0248)
 7,12-DIMETHYLBENZ(A)ANTHRACENE, CARCINOMA (1323)

- 9,10-DIMETHYL-1,2-BENZANTHRACENE,
SARCOMA, CARCINOMA, VAGINA (0441)
DYSPLASIA, AZATHIOPRINE, HUMAN (0692)
DYSPLASIA, CARCINOMA IN SITU, TRANSI-
TION TIME (1157)
DYSPLASIA, RENAL TRANSPLANTATION,
IMMUNOSUPPRESSIVE DRUGS (0693)
EPITHELIUM, HERPES SIMPLEX, HUMAN
(0620)
EPITHELIUM, MORPHOLOGY, CARCINOGENESIS
HUMAN (0853)
ESTRADIOL, DIETHYLSTILBESTROL,
EPITHELIAL CHANGES, MONKEYS (1769)
HERPES, CANCER, REVIEW (1755)*
HISTOCHEMICAL CHANGES, MALIGNANT
TRANSITION (1595)
HYPERPLASIA, ORAL CONTRACEPTIVES
(2478)*
INVASIVE CARCINOMA, HERPESVIRUS
TYPE 2, ANTIBODIES (0624)
MALIGNANCY, ORAL CONTRACEPTIVE,
DEPO-MEDROXYPROGESTERONE ACETATE
(1832)
MALIGNANT PROGRESSION, CYTOLOGICAL
SCREENING (1620)
MONKEY, CHRONIC ESTROGENIC STIMULA-
TION, EPIDERMIZATION OF ENDOMETRIUM
(1158)
MUCOUS LUBRICATION, 3-METHYLCHOL-
ANTHRENE, MOUSE (2235)
MYCOPLASMA, SQUAMOUS CELL (0282)
POLYPS, HYPERESTRINISM, ENDOMETRIAL
HYPERPLASIA (0742)
PRECANCEROUS CONDITION, CHROMOSOME
(2467)
SQUAMOUS CELL CARCINOMA, POSTMENO-
PAUSAL WOMEN, CYTOLOGIC FEATURES
(0313)
SQUAMOUS CELL CARCINOMA, SKIN
CARCINOMA, TANZANIA (1176)
SQUAMOUS CELL CARCINOMA, TS ANTIGENS,
OVARIAN CYSTADENOCARCINOMA (2000)
VAGINA, DIETHYLSTILBESTROL, EPITHELIUM
(1294)
VAGINAL TRICHOMONIASIS, PRECANCEROUS
CONDITION (1238)
- CHALONE
EPIDERMAL, HAMSTER, SQUAMOUS CELL
CARCINOMA (1216)
EPIDERMAL, SQUAMOUS CELL CARCINOMA,
HAMSTER (1208)
- CHEMICAL CARCINOGEN
AROMATIC HYDROCARBONS, ELECTRON
TRANSFER ENERGY, HYDROPHOBIC PROTEIN
BINDING, STATISTICAL ANALYSIS (2153)
BACTERIOPHAGE T4, MUTAGENICITY (0400)
BINDING TO CELL PROTEIN, TARGET ORGAN
SPECIFICITY, REVIEW (0833)
CR, AS, NI, AROMATIC HYDROCARBONS,
AZO DYES, RADIATION, OCCUPATIONAL
HAZARDS, REVIEW (0878)*
DIETHYLNITROSAMINE, FISH, REVIEW
(2167)*
DIMETHYLNITROSAMINE, BACTERIAL
SYNTHESIS (1346)
DNA BINDING (2149)
ENVIRONMENT, COOPERATIVE RESEARCH
EFFORT (0377)*
- FOOD ADDITIVES, PESTICIDES, ENVIRON-
MENTAL HUMAN CANCER (1275)
IMMUNOLOGY, REVIEW (0361)
GENETIC ACTION, HUMAN ENVIRONMENT
(2168)*
INDUSTRIAL, PULMONARY TUMORS, RODENTS
PRIMATES, REVIEW (1749)
INDUSTRIAL, TUMOR MORPHOLOGY, LUNG
TUMORS (1750)
LABORATORY WORKER, BLADDER CARCINOMA
(0367)
LIVER, PROTEIN SYNTHESIS (2151)
MONONITROQUINOLINES, ELECTRONIC
STRUCTURE, HUCKEL (1826)
NATURALLY OCCURRING, SYMPOSIUM REVIEW
(1285)*
NITROSAMINES, CYSTEINE S-CARBOXYL
DERIVATIVES, LUNG CARCINOGENS
(0083)
NON-MALIGNANT MORTALITY, TOPICAL
ADMINISTRATION (1191)*
POLYCYCLIC THIAZOLE CARCINOGENS
(2269)*
POLYMER, SARCOMA RAT (0488)
PROTEIN TARGETS, PRINCIPAL PROTEIN
CONJUGATES (0050)
SMOKED FOOD PRODUCTS, REVIEW (0879)*
SYNTHESIS, 15,16-DIHYDRO-7-METHYL-
CYCLOPENTA(A)PHENANTHRENE-17-ONE
(1763)
TERATOGEN, CHEMICAL POLLUTANT (0518)
TRANSFORMATION, REVIEW (0390)*
TUMOR ANTIGENICITY (0843)
VIRUS PRODUCTION BY INFECTED CELLS,
X-IRRADIATION (1424)
- CHEMICAL CARCINOGENESIS
CYTOTOXIC EFFECT, CELL-CARCINOGEN
INTERACTION, REVIEW (0346)
PROTEIN COMPLEXES, ACTIVITY, OVERLAP
INTEGRALS (0348)
- CHEMOTACTIC AGENT
CANCER CELL FACTOR, MIGRATION,
INVASION (1682)
MICE, HEPATOMA CELLS (0306)
- CHILDREN
ACUTE LYMPHOCYTIC LEUKEMIA,
EPIDEMIOLOGY (1603)
BURKITT'S LYMPHOMA, TUMORS OF HEAD A
NECK (1188)
CANCER, EPIDEMIOLOGY, ITALY (2055)*
CANCER, LEUKEMIA, X-IRRADIATION (1603)
CHROMOSOMAL CHARACTERISTICS, NEURO-
GENIC TUMORS (0804)
CONGENITAL ANIRIDIA, HAMARTOMA,
SIMULTANEOUS OCCURRENCE WITH WILMS
TUMOR (1709)*
FATHER AND SON OCCURRENCE, COLORECTAL
CARCINOMA (1696)
LEUKEMIA, DOG BITE (2133)
NEOPLASMS, SEROLOGICAL STUDY (2021)*
RADIUM EXPOSURE, BONE CANCER INDUCI
(1000)
THYMIC IRRADIATION, TUMORS (1396)
THYROID CARCINOMA, EPIDEMIOLOGY AND
CLINICAL COURSE (1173)
- CHLORAMBUCIL
MYELOMONOCYTIC LEUKEMIA, CHRONIC
LYMPHOCYTIC LEUKEMIA (1365)

SERUM, BONE MARROW, PROLIFERATION, RAT (0901)
 ORAMPHENICOL
 MEDULLAR APLASIA, ACUTE LEUKEMIA, CASE REPORT (1375)*
 RAT HEPATOCARCINOGENESIS, 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE (1316)
 ORNAPHAZINE
 HODGKIN'S DISEASE, CANCER OF THE BLADDER (0110)
 PEROXIDASE ACTIVITY, RAT (1650)
 ORPROMAZINE
 INHIBITION OF CARCINOGENESIS, 7,12-DIMETHYLBENZ(A)ANTHRACENE (0452)
 ORPROPAMIDE
 LIPOMA (1830)
 ALPHA-CHOLEST-6-ENE
 5-ALPHA-CHOLESTA-1,3,6-TRIENE, TUMORIGENESIS IN MICE (0888)
 ALPHA-CHOLESTA-1,3,6-TRIENE
 TUMORIGENESIS IN MICE, 5-ALPHA-CHOLEST-6-ENE (0888)
 LESTEROL
 BIOSYNTHESIS, MORRIS HEPATOMA (2548)
 CARCINOGENESIS EXPERIMENT DESIGN, SODIUM CYCLAMATE (0512)*
 DIET, LIPID, NEOPLASM, PITUITARY, LUNG (0397)
 GALLBLADDER, CARCINOMA, DIMETHYL-NITROSAMINE, HAMSTER (1347)
 3-METHYLCHOLANTHRENE, LECITHIN (1338)
 SERUM, PARENTAL CANCER MORTALITY, EPIDEMIOLOGY (1625)
 RIOCARCINOMA
 INCIDENCE IN SWEDEN, HYDATIDIFORM MOLE, INVASIVE MOLE (0753)
 ROMATIN
 METHYLASE, HISTONE (2097)
 PROTEINS, NAEL-EXTRACTABLE, 3-METHYLCHOLANTHRENE, RAT LIVER (1337)
 RNA, LIVER, HEPATOMA, RAT (2198)
 SEX, RADIATION, ENDOMETRIAL CANCER (0810)
 ROMOSOME
 ABERRATION, ADENOVIRUS, VIRUS (0686)*
 ABERRATION, CHROMATID TYPE ABNORMALITIES, FANCONI'S APLASTIC ANEMIA (1220)
 ABERRATION, COBALT 60 IRRADIATION, 3H-URIDINE IRRADIATION (0521)
 ABERRATION, CYCLOPHOSPHAMIDE BURKITT'S LYMPHOMA CELLS (1364)
 ABERRATION, EPSTEIN BARR VIRUS (2307)
 ABERRATION, HUMAN BLOOD CELL CULTURES, ULTRASOUND EXPOSURE (0527)
 ABERRATION, LYMPHOCYTE, CYCLAMATE (0418)
 ABERRATION, LYMPHOCYTE, RADIATION, HUMAN (1008)
 ABERRATION, MALIGNANT TUMORS, PERIPHERAL BLOOD CULTURE (0330)
 ABERRATION, NEUTRON IRRADIATION, PIG LEUKOCYTES (1005)
 ABERRATION, PAGET'S DISEASE, SIMIAN VIRUS 40 (0245)
 ABERRATION, POLYCYTHEMIA, HUMAN (2531)
 ABERRATION, SMALL G, ATOMIC BOMB SURVIVORS (0541)

ABERRATION, SV40, MYCOPLASMA (0665)
 ABERRATION, VACCINIA VIRUS, HUMAN LYMPHOCYTES (1879)
 ABERRATION, VIRAL INDUCTION, VIRUS (0866)*
 ABERRATION, X-IRRADIATION, MYXOVIRUS INFECTION (1002)
 ABERRATION, X-IRRADIATION, RABBIT, HUMAN (2280)
 ABERRATION, X-IRRADIATION IN UTERO, LEUCOCYTOSIS (0538)
 ABERRATION, YOSHIDA SARCOMA CELL, 4-NITROQUINOLINE-1-OXIDE (0097)
 ABNORMALITIES, BENZENE, BONE MARROW (0030)
 ABNORMALITIES, HUMAN LEUKEMIA, INCREASED ERYTHROID MITOSES (1686)
 ABNORMALITIES, LARGE INTESTINE, POLYPS, CARCINOMA (0325)
 ABNORMALITIES, ORAL CONTRACEPTIVES (0503)
 ABNORMALITY, FIBROBLASTIC PROLIFERATION, ACUTE MYELOFIBROSIS (1247)
 ABNORMALITY, LEUKEMIA (2577)*
 ABNORMALITY, LEUKEMIA, REVIEW, HUMAN (2175)*
 ABNORMALITY, MYELOMA, HUMAN (0797)
 ABNORMALITY, VIRUS, HERPES SIMPLEX (2342)
 ABNORMALLY LAR75, 30L389C9N5, WALDENSTROM'S MACROGLOBULINEMIA (1688)
 ADENOCARCINOMA OF THE CERVIX UTERI (0254)
 ALTERATION, CERVICAL CARCINOMA (0809)
 ALTERATION, 4-NITROQUINOLINE-1-OXIDE, 4-HYDROXYAMINOQUINOLINE-1-OXIDE, HAMSTER EMBRYONIC CELL (0098)
 ALTERATION, PLASMA CELL TUMOR, FREUND ADJUVANT (0102)
 ALTERATION IN NUMBER, MYELOMA, MSCP-1 TUMOR, MOUSE (0716)
 ANOMALIES, CHRONIC MYELOID LEUKEMIA, PHILADELPHIA (1280)
 ANOMALIES, LYMPHOPROLIFERATIVE SYNDROME, ATYPICAL DYSGLOBULINEMIA, MAN (0343)*
 ANOMALIES, NEPHRO2LASTOMA, 9N61NTS, KARYOTYPE (1685)
 ANOMALY, DNA REPAIR SYNTHESIS, 4-NITROQUINOLINE-1-OXIDE, HUMAN, HAMSTER (0968)
 ANOMALY, NEOPLASTIC TISSUE, COMPUTER ANALYSIS (1256)
 ANOMALY, PLASMOCYTIC LEUKEMIA, CASE REPORT (1713)*
 ASCITES TUMOR, MOUSE (2538)
 ASCITIC SARCOMA, 3-METHYLCHOLANTHRENE, HAMSTER (1219)
 BONE MARROW, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, LEUKEMIA (0061)
 BREAKAGE, LEUKEMIA, INHERITED DISEASES (0856)
 C-GROUP, LEUKEMIC REACTION, MYELOPROLIFERATIVE DISEASE (0799)
 C MARKER, EPSTEIN-BARR VIRUS (0576)
 CELL FUSION, L CELLS, EHRlich, ASCITES (2554)

CHANGES, TOLUENE, BENZENE,
 OCCUPATIONAL HAZARD (2193)
 CHRONIC LYMPHOCYTIC LEUKEMIA, TRANS-
 LOCATION, GAMMA GLOBULIN (0234)
 DAMAGE, BONE MARROW, TRENIMON, NUCLEI,
 HAMSTERS (0903)
 DAMAGE, CHEMICAL, REVIEW, HUMAN
 (2174)*
 DAMAGE, CYTOGENESIS, LEAD EXPOSURE
 (0112)
 DAMAGE, X-IRRADIATION, ¹³¹I, HUMAN
 (2283)
 DNA, ASCITES, HEPATOMAS (1691)
 DNA, OVARIAN NEOPLASIA, HUMAN
 (2536)
 DOWN'S SYNDROME, BLOOM'S SYNDROME,
 LEUKEMIA, REVIEW (1756)*
 DQ-- AND DR--, RETINOBLASTOMA,
 DEVELOPMENTAL ABNORMALITIES (0806)
 E16, HUMAN MALIGNANCY (2095)
 FEMALE TUMOR KARYOTYPE, BURKITT'S
 LYMPHOMA (1697)
 FIBROBLASTS, SARCOMA, HYBRIDIZATION,
 MURINE (2386)
 GASTROINTESTINAL TRACT, TUMOR (2586)*
 GLIOMA, DOUBLE-MINUTE, HUMAN (1260)
 HEMATOLOGICAL DISORDERS, PRELEUKEMIA
 (0800)
 HERPES SIMPLEX VIRUS, L CELLS, HEP2
 (1921)
 HUMAN MALIGNANCY, ENVIRONMENTAL
 CARCINOGEN (2101)
 HYBRIDIZATION, EHRLICH TUMOR,
 TUMORIGENICITY (2514)
 HYPERDIPLOIDY, MENINGIOMAS, HUMAN
 (1692)
 KARYOTYPE, LYMPHOBLASTOID CELLS IN
 VITRO, ACUTE LEUKEMIA (1693)
 KARYOTYPE, NEUROGENIC TUMORS, CHILDREN
 (0804)
 KARYOTYPE, TUMOR TRANSPLANTABILITY,
 FERRIDEXTRAN SPOFA-INDUCED SARCOMA
 (0706)
 KARYOTYPE ANALYSIS, ABERRATIONS,
 SPORADIC RETINOBLASTOMA (0805)
 KARYOTYPE STUDIES, CHLOROBLASTOMA,
 GRANULOCYTIC LEUKEMIA, RAT (1803)
 KARYOTYPES OF TUMOR CELLS, ROUS
 SARCOMA VIRUS (0591)
 LEUKEMIA, PANCYTOPENIA, BENZENE
 (2273)*
 LEUKEMOGENESIS, GROSS VIRUS, MICE
 (1904)
 LONG ACROCENTRIC MARKER, SOLID TUMORS,
 MALIGNANT EFFUSIONS (2098)
 LUNG, SV40, HAMSTER (1498)
 MENINGIOMA, HUMAN (2519)
 METAPHASE, DNA, EPSTEIN-BARR VIRUS
 (1881)
 METAPHASE ABERRATIONS, HAMSTER LIVER
 CELLS, COBALT 60 (1394)
 METAPHASE DEFECTS, L-CYSTEINE,
 PROTECTIVE ACTION (1360)
 N-METHYL-N'-NITRO-N-NITROSOGUANIDINE,
 CELL CYCLE, EMBRYONIC LUNG CELL
 (0484)
 MICRO-, HUMAN MYELOMONOCYTIC LEUKEMIA,
 BONE MARROW (1147)

MISSING G GROUP, ATYPICAL KARYOTYPE
 CHRONIC MYELOGENOUS LEUKEMIA (169)
 MITOSIS, RNA, DNA (2072)
 MODALITY, HEPATOMA, CYSTEINE
 DESULFURASE, BETA-MERCAPTOPYRUVAT
 DESULFURASE, RAT (0807)
 MODALITY, REVERSION, SV40 VIRUS,
 POLYOMA VIRUS, MOUSE CELL LINE
 (0558)
 MURINE SARCOMA -180, L-5178Y LYMPHO
 BLAST (1661)
 MUTATION, AZATHIOPRINE, METAPHASES,
 OXIMAZON (1766)
 MUTATION, DIMETHYLBENZANTHRACENES,
 DROSOPHILA MELANOGASTER (0439)
 NEUROBLASTS, X-IRRADIATION, DN1
 SYNTHESIS (1391)
 NORMAL, MEDULLARY THYROID CARCINOMA
 (1710)*
 PATTERN, TRANSITIONAL CELL TUMOR,
 HUMAN (2099)
 PHILADELPHIA, ACUTE LYMPHOCYTIC
 LEUKEMIA (0130)
 PHILADELPHIA, CHRONIC MYELOCYTIC
 LEUKEMIA (1730)
 PHILADELPHIA, CHRONIC MYELOID LEUKE
 CYTOGENETICS, CARCINOGENESIS (034)
 PHILADELPHIA, CHRONIC MYELOID LEUKE
 POLYCYTHEMIA (0010)
 PHILADELPHIA, LEUKEMIA (1753)*
 PHILADELPHIA, MENINGIOMA, HUMAN (25)
 PHILADELPHIA, Y, MYELOID LEUKEMIA,
 CASE REPORT (1721)*
 PH1, ACUTE MYELOBLASTIC LEUKEMIA, D
 GUGLIELMO'S SYNDROME (1252)
 PH1, ANEUPLOIDY, ACUTE MYELOGENOUS
 LEUKEMIA (0798)
 PH1, CHROMOSOME-NEGATIVE MARROW CEL
 CHRONIC MYELOCYTIC LEUKEMIA (1235)
 PH1-LIKE, FAMILIAL TRANSMISSION
 (1719)*
 PRECANCEROUS CONDITION, CERVIX, HUM
 (2467)
 RESISTANT GENE, FRIEND LEUKEMIA VIR
 (0169)
 RETICULOSARCOMA, CLONAL PROLIFERATI
 (1224)
 RHABDOMYOSARCOMA, DOUBLE-MINUTE,
 HUMAN (2525)
 ROUS SARCOMA VIRUS, POLYOMA VIRUS,
 HAMSTER CELLS (2364)
 ROUS SARCOMA VIRUS, RAT (1084)
 SEX, GONADAL DYSGENESIS, AMENORRHEA
 MALIGNANCY (1261)
 THIOACETAMIDE, LIVER (1297)
 THOROTRAST, PERIPHERAL, ABERRATIONS
 LYMPHOSARCOMA (0137)
 TRANSLOCATION INDUCTION, MOUSE
 SPERMATOGONIA, X-IRRADIATION
 (1392)
 TRISOMY, SV40, SUSCEPTIBILITY (2375)
 TUMOR, POLYPASSAGE, 3-METHYLCHOL-
 ANTHRENE, HAMSTER (2236)
 VIRUS, BOVINE KIDNEY CELLS, HAMSTER
 LUNG CELLS (1491)
 COBALT ALLOY
 WEAR PARTICLES, PROSTHESIS, TUMOR
 INDUCTION (1853)

CARCINOGEN
 MALARIAL PARASITE, BURKITT'S LYMPHOMA (0690)*
 PHORBOL MYRISTATE ACETATE, PROMOTER (0398)
 CHICINE
 WALDENSTROM'S MACROGLOBULINEMIA, ABNORMALLY LARGE CHROMOSOME (1688)
 ON
 ADENOCARCINOMA, CARCINOEMBRYONIC ANTIGEN, LOCALIZATION (0235)
 CARCINOMA, DIMETHYLHYDRAZINE, INGESTA, RATS (2215)
 CARCINOMA, FAMILIAL POLYPOSIS, HYDROLYTIC ENZYME DISTRIBUTION (0337)
 CARCINOMA, URETEROSIGMOIDOSTOMY, MAN (0825)*
 DESMOID TUMORS, POLYPOSIS COLI (1156)
 FAMILIAL POLYPOSIS, TERMINAL ILEUM, POLYPOID LYMPHOID HYPERPLASIA (0827)*
 JUVENILE POLYPS, ALLERGY, FAMILIAL (0326)
 LEUKEMIA, FAMILY 'G', INCIDENCE (2533)
 PROLIFERATING CELLS, NEOPLASTIC LESION, NUCLEIC ACID METABOLISM (2076)
 STATISTICS, HUMAN (0281)
 STOMACH, ARGYROPHIL CELLS, NEOPLASIA (1590)
 CANAVALIN A
 AGGLUTININ, CONTACT INHIBITION, POLYOMA VIRUS (0679)
 UNJUNCTIVA
 MALIGNANT MELANOMA (0749)*
 UMARIN
 AFLATOXINS, FURAZOLIUM, GUNIEA PIG, HYPERSENSITIVITY (0424)
 OTON OIL
 BETA-GLUCURONIDASE, RAT (2180)
 MAST CELL, INFLAMMATION, RAT (2182)
 PHORBOL DERIVATIVES, TRITIUM LABELING TECHNIQUE (0516)*
 SKIN TUMOR, UV IRRADIATION, ACETIC ACID, XYLENE (0545)
 THYMIDINE INCORPORATION, 13-0-TETRADECANOYL-PHORBOL-12-ACETATE (0892)
 OWN GALL
 GENETIC INFORMATION, NUCLEAR DNA, BACTERIAL DNA, TUMOR TISSUE (1254)
 TERATOMA, GLUTAMINE (1694)
 CASIN
 DIET, LIVER, MORTALITY (2490)
 HAMSTER LIVER TUMORS, NEWBORN AND ADULT HAMSTERS (1765)
 LIVER TUMORS, PULMONARY TUMORS (0895)
 CLAMATE
 CYCLOHEXYLAMINE, URINARY EXCRETION IN HUMANS (1771)
 HEPATOMAS, PULMONARY TUMORS, MOUSE, REVIEW (0378)*
 LYMPHOCYTES, CHROMOSOME ABERRATIONS (0418)
 METABOLISM IN RAT, DIET (0419)
 RAT BLADDER TUMORS, RESTRICTION OF PUBLIC CONSUMPTION (0420)
 SACCHARIN, ENVIRONMENTAL FACTOR, CARCINOGENICITY, REVIEW (2171)*
 CYCLOHEXIMIDE
 DNA SYNTHESIS, POLYOMA VIRUS, MOUSE EMBRYO CELL (1110)
 CYCLOHEXYLAMINE
 MUTAGENESIS, LEUKOCYTE, HUMAN (2203)
 SODIUM CYCLAMATE, URINARY EXCRETION IN HUMANS (1771)
 CYCLOPHOSPHAMIDE
 BLADDER CARCINOMAS, N-2-FLUORENYL-ACETAMIDE DIET (1302)
 BURKITT'S LYMPHOMA CELLS, CHROMOSOMAL ABERRATION (1364)
 LUNG ADENOMA, CARCINOMA, TRANSPLACENTAL EFFECT, MOUSE (2185)
 METASTASIZING OVARIAN CARCINOMA, ACUTE MYELOGENOUS LEUKEMIA (0506)
 CYST
 DENTAL, JAW, AMELOBLASTOMA (0244)
 CYSTEAMINE
 CHINESE HAMSTER LUNG CELLS, IRRADIATION, MITOTIC DELAY, CHROMOSOMAL ABERRATION (0129)
 CYSTEINE S-CARBOXYL DERIVATIVES
 NITROSAMINES, LUNG CARCINOGENS (0083)
 CYTOGENESIS
 LEAD EXPOSURE, CHROMOSOME DAMAGE (0112)
 CYTOGENETICS
 LEUKEMIA, HUMAN, ACUTE GRANULOCYTIC (2582)*
 LYMPHOID CELL LINES, EPSTEIN-BARR VIRUS (1884)
 3-METHYLCHOLANTHRENE, MOUSE MAMMARY CARCINOMA (1340)
 CYTOSINE ARABINOSIDE
 HERPES SIMPLEX, CHROMOSOME CHANGES, HUMAN (2339)
 CYTOTOXIC REACTION
 MASTOCYTOMA CELLS, PHOSPHOLIPID METABOLISM (2057)
 CYTOTOXICITY
 SERUM FRACTION ANTIBODIES, GROUP SPECIFIC ANTIGENS, RAUSCHER VIRUS, MOUSE (1448)
 SPLEEN CELLS, RHABDOMYOSARCOMA, MOUSE (2432)
 SV40, ANTI-MOUSE EGG ANTIGEN (0669)
 DAIRY PRODUCT
 CONSUMPTION, BREAST CANCER MORTALITY, REGIONAL VARIATIONS IN ENGLAND (2047)
 DDT
 CHLOROPHENOTHANE, ACUTE LEUKEMIA, OCCUPATIONAL EXPOSURE (0509)
 DEOXYCHOLATE
 CANCER IMMUNITY, HUMANS, ANIMALS (2465)*
 DEPIGMENTATION
 EFFECT, 9,10-DIMETHYL-1,2-BENZANTHRA-CENE, EPIPHYSECTOMY, BENZANTHRACENE, HAMSTER (0444)
 DEPO-MEDROXYPROGESTERONE ACETATE
 CERVICAL MALIGNANCY, ORAL CONTRACEPTIVE (1832)
 DERMATOGLYPHIC PATTERNS
 LEUKEMIA, GENETIC FACTOR (0363)

DESMOSTEROL
 NERVOUS SYSTEM TUMORS, NITROSUREA,
 RAT (0089)
 DIBENZACRIDINE
 CARCINOGENIC POTENCY, STRUCTURE
 ACTIVITY RELATIONSHIPS, CHEMICAL
 DISPLACEMENTS, SUPERDISLOCABILITY
 INDEX (0520)*
 DIBENZ(A,H)ANTHRACENE
 METABOLISM, EPOXIDE INTERMEDIATE,
 LIVER, RAT (2221)
 K-REGION EPOXIDE, PHENANTHRENE, DNA,
 RNA (0067)
 DIBENZOPYRENE
 TRICAPRYLIN, ADENOMA, LIMONENE, MOUSE
 (1795)
 DIBUTYLNITROSAMINE
 BLADDER, TUMOR, MOUSE (0481)
 SYRIAN AND CHINESE HAMSTERS, CARCINOMA
 DEVELOPMENT (1351)
 URINARY BLADDER TUMORS, ALKALINE
 PHOSPHATASE, RAT (2024)
 3,3'-DICHLORO-4,4'-DIAMINO-DIPHENYL-ETHER
 CARCINOGENICITY, AUDITORY CANAL, RAT
 (1767)
 DIET
 CIRRHOSIS, LIVER CARCINOMA, RAT (2471)
 CYCLAMATE, METABOLISM IN RAT (0419)
 FEED, CONTAMINATION, AFLATOXINS B1,
 B2, G1, G2 (0991)*
 IMMUNITY, TUMOR HETEROGRAFT, RAT
 (2401)
 LIPOTROPE-DEFICIENT, LIVER TUMORS,
 AFLATOXIN CARCINOGENESIS (0915)
 MEXICAN POPULATION IN TEXAS, GALL-
 BLADDER CANCER, ETIOLOGY (1171)
 POLYUNSATURATED FAT-RICH DIET,
 CARCINOMA MORTALITY (1363)
 RENAL TUMORS, DIMETHYLNITROSAMINE,
 RATS (0952)
 SMOKED FISH, JAPAN, BENZO(A)PYRENE
 (2202)
 DIETARY FAT
 TUMOR INCIDENCE, 7,12-DIMETHYLBENZ(A)
 ANTHRACENE, DOSE (0062)
 DIETHYLAMINOETHYL-DEXTRAN
 MURINE SARCOMA VIRUS, TUMOR
 ENHANCEMENT (2351)
 DIETHYLNITROSAMINE
 GLUCOSE-6-PHOSPHATASE, HORMONE, LIVER,
 RABBIT, RAT (1814)
 HEPATOMAS, STAGES IN MALIGNANT TRANS-
 FORMATION (0957)
 LACTATING HAMSTERS, TUMOR INDUCTION
 IN OFFSPRING (1813)
 LIVER, CYCLOHEXIMIDE, RAT (1372)*
 LIVER, ENZYME HISTOCHEMISTRY, RAT (0960)
 LIVER, HEPATECTOMY, REGENERATION, RAT
 (0959)
 LIVER, SPLEEN, KARYOTYPE, RAT (2243)
 LIVER CANCER, IMMUNOSUPPRESSION, RAT
 (1815)
 LIVER CELL, NUCLEAR MEMBRANE
 PERMEABILITY, RAT (0081)
 LUNG ADENOMA, HEPATIC DAMAGE, MICE
 (2245)
 MICE, TUMOR TYPES, ORGAN SUSCEPTI-
 BILITY (1348)
 PAPILLOMAS, TRACHEAL MUCOSA,
 HAMSTERS, NUCLEIC ACID (1349)
 PAPILLOMATA, TRACHEAL MUCOSA, CYTO-
 PHOTOMETRY, GOLDEN HAMSTER (0480)
 PULMONARY CARCINOGENESIS, GOLDEN
 HAMSTER, ORGANOTROPY (1345)
 RENAL TUMORS, PARTIAL HEPATECTOMY,
 RAT (1812)
 RIBOSOMAL FERRITIN, RAT LIVER (047)
 SORBITOL DEHYDROGENASE, LIVER, RAT
 (0085)
 TRACHEA, HAMSTER (2242)
 TRANSPLACENTAL EFFECT, LIVER NECROSIS
 PNEUMONIA, RAT (1811)
 TRANSPLACENTAL EFFECT, LUNG ADENOMA
 MOUSE (1816)
 DIETHYLSTILBESTROL
 CERVIX, VAGINA, EPITHELIUM (1294)
 CHICKEN LIVER, LYSYL-TRANSFER RNA
 (1205)
 DNA SYNTHESIS, LEYDIG-CELL TUMOR
 (0022)
 NEPHROBLASTOMA, ULTRASTRUCTURE
 HAMSTER (1373)*
 DIETHYL-SULFATE
 NERVOUS SYSTEM TUMORS, DIMETHYL-
 SULFATE (0032)
 DIFFERENTIATION
 CELL COLONY-FORMING ABILITY, FRIEND
 LEUKEMIA VIRUS (0603)
 MALIGNANT, BENIGN, SQUAMOUS CELL
 CARCINOMA, RAT (1588)
 MAMMARY GLAND, LOBULOALVEOLAR, MICE
 STRAIN DIFFERENCES, HORMONE (0769)
 PAPILLARY FOLLICULAR THYROID TUMOR,
 IMPLANTS, RAT (2562)
 TRACHEAL MUCOSA, DIETHYLNITROSAMINE
 GOLDEN HAMSTER, TRACHEAL MUCOSA
 (0480)
 TROPHOBLASTIC, GONADOTROPHIN SECRET
 BRONCHIAL CARCINOMA (0774)
 UNDIFFERENTIATED SUBENDOTHELIAL CEL
 SWINE AORTA, HYPERLIPEMIC DIET
 (0261)
 DIGESTIVE TRACT
 TUMOR SPECIFIC ANTIGENS, ALPHA-
 FETOGLOBULIN (0362)
 DIGIT FIBROUS TUMOR
 CYTOPLASMIC INCLUSIONS, VIROLOGICAL
 STUDY (0795)
 2,5-DIMETHOXY-4-AMINOAZOBENZENE
 HEPATOMA, TARGET ORGANS, DOSE EFFECT
 RAT (0055)
 DIMETHYLAMINOAZOBENZENE
 ANTIGENS, HEPATOMA, RAT (2423)
 CARCINOGENESIS INHIBITION, NAPHTHYL
 THIOCYANATE, LIVER, RAT (0433)
 DIETHYLAMINOAZOBENZENE, HEPATOMA,
 ANTIGENS (0434)
 METABOLITES, DNA BINDING, RAT LIVER
 MICROSOMES (0921)
 TUMOR, HEPATECTOMY, HYPERTROPHY,
 RAT (2214)
 4-DIMETHYLAMINOAZOBENZENE
 AZO DYE REDUCTASE, RAT LIVER, CECAL
 BACTERIA (0054)
 IMMUNE RAT LYMPH NODES, HEPATOMA
 (1550)

LYSOSOMAL ENZYME ACTIVITY, RAT LIVER
 LYSOSOMES (1784)
 MITOTIC RATES, LIVER CELL PARENCHYMA
 (1782)
 DIMETHYL-4-AMINOAZOBENZENE
 DAB-REDUCTASE, RAT LIVER (1315)
 DIMETHYLAMINOAZOBENZENE
 N,N'-DIMETHYL-P-PHENYLAZOANILINE,
 CARCINOGENIC ACTIVITY, ELECTRON
 DENSITY STUDIES (0029)
 LIVER, SYNESTROL, TESTOSTERONE, RAT
 (1314)
 LIVER CHANGES, ENZYME ACTIVITY, RAT
 (0922)
 MICE AND HAMSTERS, AZODYE BINDING TO
 LIVER PROTEINS (0923)
 PHOSPHOFRUCTOKINASE, LIVER, RAT
 (1318)
 PREGNENOLONE, LIVER CANCERIZATION,
 RATS, HYPOTHALAMUS (1313)
 DIMETHYLAMINOPHENYLAZODIBENZOTHIOPHENE
 CARCINOGENICITY IN RAT LIVER (0924)
 DIMETHYLAMINOSTILBENE
 SKIN TUMORS, RAT (0470)
 N,N'-4-DIMETHYLAMINOSTILBENE
 EAR DUCT TUMOR, LEUKEMIA, RATS (0031)
 ETHYLBENZANTHRACENE
 ESTROUS CYCLE, RESERPINE, MAMMARY
 GLAND CARCINOMA, RAT (1794)
 SKIN, HAMSTER, MELANOMA (0118)*
 TRYPAN BLUE, HODGKIN'S DISEASE,
 PATHOGENESIS, REVIEW (0019)*
 ETHYLBENZ(A)ANTHRACENE
 LYMPHATIC URIDINE UPTAKE, ANTI-
 LYMPHOCYTE SERUM (0456)
 MAMMARY GLAND, CARCINOMA, RAT, INSULIN
 (0450)
 TESTOSTERONE, MAMMARY ADENOCARCINOMA
 (0448)
 2-DIMETHYLBENZANTHRACENE
 BREAST CANCER, ESTROGEN, RAT (0064)
 DOSE, LOW FAT DIET, TUMOR INCIDENCE
 (0062)
 GERM-FREE STATE, TUMOR PROTECTION
 (0065)
 LEUKEMIA, BONE MARROW CHROMOSOME (0061)
 LIVER, ADRENAL (0066)
 MAMMARY TUMORS, HORMONE RESPONSIVENESS
 (0060)
 NUCLEIC ACID SYNTHESIS, LIVER
 REGENERATION (0058)
 PROTEASE INHIBITOR, TUMORIGENESIS
 PROMOTER (0059)
 SALIVARY GLAND NEOPLASM, ENVIRONMENT,
 VITAMIN A, RAT (0308)
 SKIN GRAFT, TUMOR, HETEROGENIZATION
 (0057)
 SUPPLEMENTARY ASSAY, NEOPLASM (0063)
 2-DIMETHYLBENZ(A)ANTHRACENE
 ADRENAL LESION, MUSCULAR STRESS, RAT
 (2217)
 ADRENALS, NECROSIS, STEROID, RAT
 (0438)
 7-BROMO-METHYL-12-METHYLBENZANTHRACENE
 1,7-DIMETHYLBENZANTHRACENE,
 3,9-DIMETHYLBENZANTHRACENE,
 CHROMOSOME, MUTATION, DROSOPHILA
 MELANOGASTER (0439)
 BUCCAL POUCH, EPIDERMOID CARCINOMA,
 ANTILYMPHOCYTE SERUM (1541)
 CANCER, LIP MUCOSA, HAMSTER (0453)
 CARCINOGENESIS, AGE DEPENDENCE, MOUSE,
 RAT (0436)
 CARCINOGENICITY, GUINEA PIGS (0437)
 CARCINOMA, CERVIX (1323)
 CARCINOMA, MAMMARY GLAND, RAT (0442)
 CASTRATED AND INTACT HAMSTERS, TES-
 TOSTERONE (0449)
 CEREBELLUM, TUMOR MODEL, RAT (2220)
 CERVIX, VAGINA (0441)
 CHLORPROMAZINE, INHIBITION OF CARCINO-
 GENESIS (0452)
 CORTISONE ACETATE, INHIBITION OF
 CARCINOGENESIS (0451)
 1,2,5,6-DIBENZANTHRACENE, IONIZING
 IRRADIATION, RARE EARTH METALS, RAT
 (2294)*
 DIGESTIVE TRACT, MOUSE (0926)
 DNA, BENZ(A)ANTHRACENE, BINDING (0934)
 DNA, CARCINOGEN BINDING, RAT LIVER
 (2224)
 EMBRYO, DNA, RNA, ACTINOMYCIN D,
 1-MERCAPTO-1-(BETA-4-PYRIDETHYL)
 BENZIMIDAZOLE (1322)
 EPIPHYSECTOMY, BENZANTHRACENE,
 DEPIGMENTATION EFFECT, HAMSTER
 (0444)
 FIBROSARCOMA, EMBRYO, HAMSTER (1331)
 GUINEA PIGS, CONTACT SENSITIVITY
 (1324)
 HORMONE, REGRESSION, PROLACTIN, RAT
 (2226)
 LEUKEMOGENESIS, PHORBOL (0893)
 LIVER, HEPATECTOMY, RAT (2218)
 MAMMARY ADENOCARCINOMA, DISTAL SMALL
 BOWEL BYPASS (1792)
 MAMMARY GLAND, CARCINOMA, IMMUNOLOGY,
 RAT (0454)
 MAMMARY GLAND, FIBROADENOMA, LACTOSE,
 RAT (2223)
 MAMMARY GLAND, HORMONAL ANTITUMOR
 THERAPY, RAT (0457)
 MAMMARY GLAND CELL NUCLEI, RNA
 POLYMERASE ACTIVITY, RAT (1791)
 MAMMARY GLAND TUMOR, ANTISERA, RAT
 (1990)
 MAMMARY NEOPLASIA, ISOENZYMES,
 OOPHORECTOMY, RAT (2222)
 MAMMARY TUMOR, PROLACTIN (0927)
 MAMMARY TUMOR ENHANCEMENT, BACILLUS
 CALMETTE-GUERIN (1243)
 MAMMARY TUMOR SUPPRESSION, ACTINOMYCIN
 D (0932)
 MAST CELLS, MAMMARY TUMORS, RAT (2227)
 MELANOID TUMORS, GOLDEN HAMSTER,
 PINEALECTOMY, SEX DIFFERENCE (1328)
 METABOLISM, OVARIAN TUMORS, MICE
 (1787)
 3-METHYLCHOLANTHRENE, POLYOMA VIRUS,
 CELL GROWTH, IN VITRO, HAMSTER
 (2194)
 METHYLTHIOURACIL, L-THYROXINE, RAT
 (1790)
 MICE, SKIN, DNA REPLICATION (0931)
 PAPILLOMA, PHORBOL ESTER ACETATE
 (1321)

- PHAGOCYTOSIS, ANTIBODY, LEUKEMIA, LIVER (1451)
 POLYINOSINIC-POLYCYTIDYLIC ACID, LYMPHOMA, THYMUS, MOUSE (2225)
 PREGNANT MICE, PULMONARY ADENOMA IN PROGENY (1332)
 RADIATION LEUKEMOGENESIS, BONE MARROW CELLS (0928)
 RAUSCHER LEUKEMIA VIRUS, CELL TRANSFORMATION (1326)
 RESERPINE, MAMMARY TUMOR (0929)
 SARCOMA, IMMUNIZATION, RAT (0455)
 SIMIAN ADENOVIRUS 7, TUMOR TRANSPLANT IMMUNITY (1982)
 SKIN, ARYL HYDROCARBON HYDROXYLASE, 7,8-BENZOFILAVONE, MOUSE (0445)
 SKIN MORPHOLOGY, MOUSE (2189)
 SKIN SUSCEPTIBILITY, HAIR FOLLICLE CYCLE, MOUSE (0443)
 SKIN TUMOR, POLYINOSINIC ACID/POLYCYTIDYLIC ACID, RNA, PHORBOL ESTER, MOUSE (0447)
 SKIN TUMOR, RIBOFLAVIN DEFICIENCY (0935)
 SQUAMOUS CARCINOMAS, ANTITHYMOCYTE SERUM (1325)
 SUSCEPTIBILITY TO TUMOR INDUCTION, HAIRLESS MICE (0446)
 SYNESTROL, OSTEOSARCOMA, RABBIT (1329)
 TESTOSTERONE, OVARICTOMY, MAMMARY GLAND TUMOR, MOUSE (1145)
 THYMIC LYMPHOMA, LEUKEMOGENIC ACTIVITY (1896)
 L-THYROXINE, METHYLTHIOURACIL, CERVICO-VAGINAL TUMORS, CASTRATION (0887)
 TOOTH SOCKET, MANDIBULAR LYMPHOMA (1788)
 TUMOR, SKIN, LUNG, MOUSE FETUS (1797)
 TUMOR REGRESSION, OVARICTOMY (1327)
 URETHAN, GAMMA-IRRADIATION, HORMONE (1789)
 URETHAN, IMMUNE RESPONSE IN RATS (1989)
 VIRUS, HERPES SIMPLEX VIRUS, VIRUS INFECTIVITY (1463)
 X-RAY IRRADIATION, SKIN TUMOR, RAT (2219)
 9,10-DIMETHYL-1,2-BENZANTHRACENE
 SQUAMOUS CELL CARCINOMA, PROLIFERATION KINETICS, IRRADIATION (0068)
 3,3'-DIMETHYLBENZIDINE
 SKIN TUMORS, SEBACEOUS GLAND, RAT (0023)
 DIMETHYLHYDRAZINE
 COLONIC CARCINOMA, INGESTA, RATS (2215)
 1,2-DIMETHYLHYDRAZINE
 ENZYME, TRNA METHYLASE, COLONIC TUMOR, MOUSE (2216)
 INTESTINAL CARCINOMA, EARLY STAGES, AUTORADIOGRAPHY (0044)
 DIMETHYLNITROSAMINE
 ANIMOACETONITRILE, METABOLISM (0961)
 CARCINOMA, GALLBLADDER, CHOLESTEROL, HAMSTER (1347)
 DIMETHYLAMINE, SODIUM NITRITE, BACTERIAL SYNTHESIS, RAT INTESTINE (1346)
 7,12-DIMETHYLBENZ(A)ANTHRACENE, MOUSE LIVER MORPHOLOGY (0081)
 HEPATOMA, ANTIGENICITY, RAT (0956)
 HISTOLOGY OF TUMORS, KIDNEY TUMORS RAT (1810)
 KIDNEY, MESENCHYMAL TUMORS, RAT (0)
 LUNG ADENOMA, LIVER HEMANGIOSARCOMA (0080)
 METABOLISM, NUCLEIC ACID METHYLATION (0473)
 MICE, TUMOR TYPES, ORGAN SUSCEPTIBILITY (1348)
 RENAL ADENOCARCINOMAS, ULTRASTRUCTURE (1809)
 RENAL CARCINOMAS, PROTEIN DEFICIENCY (0954)
 RENAL MESENCHYMAL TUMORS, PROGRESS OF NEOPLASTIC CHANGE (1808)
 RENAL TUMORS, DIET, RATS (0952)
 RIOPELLE'S TUMOR, HISTOGENESIS, REVIEW (0371)
 RNA METHYLATION, S-ADENOSYLMETHIONINE, RAT LIVER (0082)
 TESTIS, RAT (2240)
 TRANSFORMATION, REVERTANT, LIMITED LIFE-SPAN, HAMSTER EMBRYO CELL (0951)
 TRANSPLACENTAL EFFECT, EPITHELIAL HYPERPLASIA, PAPILLARY NEOPLASIA, KIDNEY, MOUSE (0477)
 ULTRASTRUCTURE, LUNG, LIVER, MOUSE (2246)
 ULTRASTRUCTURE, RENAL MESENCHYMAL TUMOR, RAT (1807)
 DIMETHYL-SULFATE
 DIETHYL-SULFATE, NERVOUS SYSTEM TUMOR (0032)
 DIMETHYLSULFOXIDE
 CARCINOGENICITY, NEGATIVE, RAT (2187)
 4(5)-(3,3-DIMETHYL-1-TRIAZENO)IMIDAZOLE
 5(4)-CARBOXAMIDE
 MAMMARY ADENOCARCINOMA, THYRONIC LYMPHOSARCOMA (0423)
 DISEASE
 AMEBIC GRANULOMA, CECUM, ADENOCARCINOMA (2123)
 DIABETES MELLITUS, CANCER INCIDENCE AND MORTALITY, PANCREATIC CANCER (1724)
 HEMATOLOGICAL DISORDER, CHROMOSOME ABNORMALITY, HUMAN, LEUKEMIA (080)
 PARASITISM, CARCINOGENESIS, BILHARZIOSIS, TOXOPLASMOSIS (1727)
 PRECURSOR ILLNESS, LUNG CANCER (220)
 SCHISTOSOMIASIS, BLADDER, CARCINOMA (0369)
 DNA
 N-ACETOXY-2-ACETYLAMINOFLUORENE, BINDING (1772)
 POLYNUCLEOTIDES (1774)
 ADENOVIRUS 12, SIZE CLASSES (2325)
 ADENOVIRUS TYPE 12, KIDNEY CELLS, INTEGRATION (1051)
 ALKYLATING AGENTS, REPAIR SYNTHESIS HELA (2254)

ALVEOLAR CELL CARCINOMA, ALVEOLAR
 MACROPHAGE (0736)
 ASCITES, HEPATOMAS, CHROMOSOMES (1691)
 BENZ(C)ACRIDINES, DIMETHYL DERIVATIVE,
 INTERACTION (2178)
 BENZ(A)ANTHRACENE, BINDING (0934)
 BENZ(A)PYRENE, PHOTO ADDUCT, UV RADIA-
 TION (0938)
 BINDING, RAT LIVER MICROSOMES,
 DIMETHYLAMINOAZOBENZENE METABOLITES
 (0921)
 CARCINOGENS, BINDING (2149)
 CHROMOSOME, OVARIAN NEOPLASIA, HUMAN
 (2536)
 CO-CULTURE, EHRlich ASCITES, CHINESE
 HAMSTER CELLS (1202)
 COMPLEX FORMATION, POLYOMA VIRUS,
 MOUSE EMBRYO FIBROBLAST (1111)
 CROWN-GALL TISSUE CULTURE, MODEL,
 TRANSFORMATION MECHANISM (0263)*
 DOUBLE-STRAND BREAKS, X-IRRADIATION,
 MURINE LYMPHOMA CELLS (0523)
 E. COLI, N-METHYL-N'-NITRO-N-NITROSO-
 GUANIDINE, METHYLATION (0485)
 EPSTEIN-BARR VIRUS, METAPHASE CHROMO-
 SOMES (1881)
 EPSTEIN-BARR VIRUS, VIRUS, BURKITT'S
 LYMPHOMA (0688)*
 3-GLUCURONIDASE, BLADDER TUMORS, HUMAN
 (2084)
 HEPATOMA, GENE AMPLIFICATION, RAT
 (2212)
 HYBRID, ADENOVIRUS TYPE 2, SV40 (1052)
 INTERFERON, POLYOMA VIRUS, TEMPERATURE
 SENSITIVE POLYOMA MUTANT, 3T3 CELL
 CULTURE (0678)
 LEUKEMIA, CHROMOSOME, HUMAN (2564)
 LEUKEMIA, MITOCHONDRIAL, FLOTATION
 DENSITY, REVIEW (1270)
 LIGASE, EXONUCLEASE, ROUS SARCOMA
 VIRUS (2368)
 LIVER, ASCITES TUMOR, ORTHOPHOSPHATE,
 THYMIDINE (1648)
 LIVER, CARCINOGEN BINDING,
 7,12-DIMETHYLBENZ(A)ANTHRACENE, RAT
 (2224)
 LYMPH NODE CELLS, PHYTOHEMAGGLUTININ,
 ANTIGEN (0238)
 MALIGNANT FIBROBLASTS, CELL CULTURE,
 MOUSE (1717)*
 MAMMARY CARCINOMA, COLLAGENASE,
 NITROGEN, INVASION (1649)
 MARCK'S DISEASE VIRUS (2310)
 METABOLISM, AFLATOXIN B1, METHYL-
 AZOXYMETHANOL-ACETATE, ETHYLNITRO-
 SOUREA (0427)
 METHYLATION, TUMOR CHROMATIN (2100)
 3-METHYLCHOLANTHRENE, MAMMARY TUMORS,
 MURINE (1802)
 5-METHYLCYTOSINE, LEUKEMIC CELLS,
 HUMAN (2530)
 MITOCHONDRIA, VIRUS, AVIAN
 MYELOBLASTOSIS, OLIGOMER (2308)
 MOLECULAR WEIGHT, TRITIATED THYMIDINE,
 LYMPHOMA, MOUSE (2291)
 4-NITROQUINOLINE-1-OXIDE, INTERACTION,
 MODEL (1825)
 4-NITROQUINOLINE-1-OXIDE, NUCLEOSIDE,

ELECTRON SPIN RESONANCE (1355)
 NUCLEAR, UV RADIATION, PHOTOCHEMICAL
 LESION, MOUSE (0536)
 PAPILLARY THYROID CARCINOMA, HUMAN
 (0789)
 POLYMERASE, AVIAN MYELOBLASTOSIS
 VIRUS, RNA (0584)
 POLYMERASE, BIRD, VIRUS (1943)
 POLYMERASE, CHRONIC LYMPHOCYTIC
 LEUKEMIA, PLASMA (2082)
 POLYMERASE, DNA-DIRECTED, VIRUS
 (0141)
 POLYMERASE, HELA, WI38 (2561)
 POLYMERASE, HUMAN UROGENITAL TUMOR
 (0331)
 POLYMERASE, INFECTED CHICK CELLS,
 MYELOCYTOMATOSIS VIRUS (1893)
 POLYMERASE, KILHAM RAT VIRUS (2300)
 POLYMERASE, LYMPHOCYTE TRANSFORMATION,
 PHYTOHEMAGGLUTININ STIMULATION,
 REPLICATION (0703)
 POLYMERASE, MURINE SARCOMA VIRUS,
 VIRUS, RNA (0634)
 POLYMERASE, RNA HYBRID, ONCOGENIC
 VIRUS (0142)
 POLYMERASE, ROUS SARCOMA VIRUS,
 CHICKEN CELL (2358)
 POLYMERASE, ROUS SARCOMA VIRUS,
 DEFECTIVE (2398)*
 POLYMERASE, ROUS SARCOMA VIRUS,
 SYNTHESIS KINETICS (1941)
 POLYMERASE, SARCOMA, MYELOBLASTOSIS,
 VIRUS (1081)
 POLYMERASE ACTIVITY, C-TYPE RNA VIRUS
 (0555)
 POLYMERASE TEMPLATE, SARCOMA-LEUKEMIA,
 VIRAL RNA-DNA HYBRID MOLECULE
 (0143)
 POLYOMA VIRUS, AT-TYPE FIBROSARCOMA,
 GC-TYPE ADENOCARCINOMA (0220)
 POLYOMA VIRUS, THERMOSENSITIVE MUTANT
 (1109)
 PRIMARY TUMOR, METASTASIS, HUMAN
 (2516)
 QUANTITATION, SV40 VIRUS-TRANSFORMED
 CELL (2373)
 REPAIR, ULTRAVIOLET RADIATION,
 XERODERMA PIGMENTOSUM (1388)
 REPAIR SYNTHESIS, CHROMOSOME ANOMALY,
 4-NITROQUINOLINE-1-OXIDE, HUMAN,
 HAMSTER (0968)
 REPAIR SYNTHESIS, VIRUS (1356)
 REPLICATION, 7,12-DIMETHYLBENZ(A)
 ANTHRACENE, SKIN, MICE (0931)
 REPLICATION, FROG VIRUS 3, VIRUS,
 GAMMA RAYS (0522)
 REPLICATION, N-HYDROXY-2-ACETYLAMINO-
 FLUORENE, BINDING (1296)
 REPLICATION, RHABDOMYOSARCOMA, ASTRO-
 CYTOMA, NEUROBLASTOMA (1230)
 REPLICATION, VIRUS, SV40, CYCLO-
 HEXIMIDS (1504)
 RNA, ALKYLATING AGENTS, REPAIR, HELA
 (2248)
 RNA, CHINESE HAMSTER, SV40 (1954)
 RNA, NUCLEIC ACID METHYLASES (2150)
 RNA IN RAT PROSTATE, PROGESTERONE,
 ESTROGEN (0889)

RNA VIRUSES (2299)
 ROUS SARCOMA VIRUS, ISOLATION (0203)
 SARCOMA -180, PROLIFERATION KINETICS (1627)
 SHOPE FIBROMA VIRUS, RK13, LACK OF HOMOLOGY (1949)
 SIMIAN PSEUDO VIRUS, MOUSE EMBRYO CELL (1094)
 SINGLE-STRANDED, DOUBLE-STRANDED, SYNTHESIS, MURINE LEUKEMIA VIRUS (1446)
 SKIN, SQUAMOUS CELL EPITHELIOMA, CYTOPHOTOMETRY (1722)*
 SV40, ADENOVIRUS 2, HYBRID VIRUS (2332)
 SV40, ETHIDIUM BROMIDE, STRUCTURE (1494)
 SV40, KIDNEY, BSC-1 CELLS, PROPERTIES (1492)
 SV40, LENGTH OF VIRAL DNA MOLECULE (1098)
 SV40, MAMMALIAN RNA POLYMERASE (1103)
 SV40, OLIGOMERS (2378)
 SV40, SUPERHELICAL, NICKED (1951)
 SV40, UPTAKE, DEAE DEXTRAN (1502)
 SV40, VARIANT, TRANSFORMATION, HUMAN FIBROBLAST CELL (1095)
 SYNTHESIS, ACETAMIDOFLUORENE DERIVATIVES (0408)
 SYNTHESIS, ACTINOMYCIN D, SV40 VIRUS (0662)
 SYNTHESIS, ADENOVIRUS, HAMSTER KIDNEY CELL, HUMAN EMBRYO LUNG CELL (1044)
 SYNTHESIS, ADENOVIRUS TYPE 12, HAMSTER (1047)
 SYNTHESIS, CELL DENSITY, EPITHELIUM (0813)
 SYNTHESIS, CHICK EMBRYO CELL CULTURE, ROUS SARCOMA VIRUS, AVIAN LEUKOSIS VIRUS (0566)
 SYNTHESIS, DENSONUCLEOSIS VIRUS, ONCOGENICITY (0221)*
 SYNTHESIS, GLUCOSE METABOLISM, LEUKEMIA AND DIABETES (0775)
 SYNTHESIS, HERPES SIMPLEX, KB CELLS (2337)
 SYNTHESIS, HYDROCORTISONE, LIVER, RAT (2262)
 SYNTHESIS, INDUCTION, SV40 (1499)
 SYNTHESIS, LEUKOCYTE, EPSTEIN-BARR VIRUS (1884)
 SYNTHESIS, LEYDIG-CELL TUMOR, DIETHYLSTILBESTROL (0022)
 SYNTHESIS, LYMPHOCYTE TRANSFORMATION, ALPHA-AMINO-P-TOLUENESULFONAMIDE, HUMAN (0508)
 SYNTHESIS, LYMPHOCYTES, LYMPHO-GRANULOMA (2584)*
 SYNTHESIS, MEGALOBlastic ANEMIA, PHYTOHEMAGGLUTININ-TRANSFORMED LYMPHOCYTE (0698)
 SYNTHESIS, MOUSE EPIDERMIS, HYDROCORTISONE, CHALONE, CROTON OIL (2059)
 SYNTHESIS, MOUSE KIDNEY CELL CULTURE, POLYOMA VIRUS, T-ANTIGEN (0676)
 SYNTHESIS, NEOPLASTIC CELLS, PHYTOHEMAGGLUTININ (1997)

SYNTHESIS, NEUROBLASTS, X-IRRADIATION (1391)
 SYNTHESIS, PARVOVIRUS H-1, SV40, THYMIDINE KINASE (0210)
 SYNTHESIS, PHYTOHEMAGGLUTININ, LYMPHOCYTES, EXTRACORPOREAL IRRADIATION OF BLOOD (0526)
 SYNTHESIS, POLYOMA VIRUS, CYCLO-HEXIMIDE, MOUSE EMBRYO CELL (1110)
 SYNTHESIS, POLYOMA VIRUS, MITOCHONDRION (1513)
 SYNTHESIS, POLYOMA VIRUS, MOUSE EMBRYO CELL (1106)
 SYNTHESIS, RNA DEPENDENT, ONCOGENESIS, NORMAL CELL DEVELOPMENT (1268)
 SYNTHESIS, ROUS SARCOMA VIRUS, IN VITRO (2357)
 SYNTHESIS, SV40, HAMSTER (1089)
 SYNTHESIS, SV40, 3T3 (1952)
 SYNTHESIS, SV40 VIRUS, THERMOSENSITIVE SV40 MUTANT, TEMPERATURE EFFECT (1090)
 SYNTHESIS, THYMIC STIMULATORY FACTOR, BONE MARROW (1657)
 SYNTHESIS, UV IRRADIATION DAMAGE, NON-PROLIFERATING ACUTE LEUKEMIA CELLS (1223)
 SYNTHESIS, VIRUS, SERUM (0216)
 SYNTHESIS, X-IRRADIATION, HAMSTER CELLS (2290)
 SYNTHESIS, X-RAY, KIDNEY, EHRLICH CELLS, LIVER (1390)
 TEMPERATURE SENSITIVE MUTANT, ADENOVIRUS 31 (1458)
 TEMPLATE, CARCINOGEN BINDING, POLYCYCLIC AROMATIC HYDROCARBONS (2266)*
 THERAPY, POLYOMA PSEUDOVIRUS, UNCOLORED, DNASE (0683)
 THERMAL DENATURATION, THYMUS, CALF, ALKYLATING AGENTS (0422)
 TRANSFORMATION SUSCEPTIBILITY, SV40 (0659)
 TUMOR, EHRLICH ASCITES (2579)*
 TUMOR, FEULGEN CYTOPHOTOMETRY, BENIGN MALIGNANT, HUMAN (1640)
 TUMOR, GENETIC INFORMATION, BACTERIAL DNA, NUCLEAR DNA (1254)
 UNSCHEDULED SYNTHESIS, MUSCLE, RAT (2201)
 VIRAL, DENSITIES, LUCKE ADENOCARCINOMA, FROG HERPESVIRUS, BURKITT'S LYMPHOMA (0621)
 VIRAL FORMS, CYCLOHEXIMIDE, SV40 (1503)
 VIRAL GENOME, TRANSFORMATION (2156)
 VIRUS, KILHAM RAT (2399)
 VIRUS, SIMIAN ADENOVIRUS, DENSITY (2296)
 VIRUS-SPECIFIED, SV40, SURFACE AND TUMOR ANTIGENS (0209)
 WALKER-256 CARCINOSARCOMA, TRANSFORMATION REVERSAL (1210)
 DUODENUM
 DIETETIC PANTHOTHIC ACID DEFICIENCY, FOCAL AVILLIOUS HYPERPLASIA, MOUSE (0311)

ST
SILICOTIC, EFFECT ON 3,4-BENZOPYRENE
INDUCING OF LUNG TUMORS, RAT (0122)*
PLASIA
CERVIX, AZATHIOPRINE, HUMAN (0692)
R
CARCINOMA, 3,3'-DICHLORO-4,4'-DIAMINO-
DIPHENYL-ETHER, RAT (1767)
DUCT TUMOR, LEUKEMIA, AMINOSTILKENE
DERIVATIVES (0031)
LY SCREENING
CANCER DETECTION, PHYSICAL EXAMINATION
(0295)*
OLOGY
CARCINOGENIC FACTORS, REVIEW (0384)*
CARCINOGENIC HYDROCARBONS, WATER
POLLUTION INDEX, BENZO(A)PYRENE,
U.S.S.R. (0515)*
LECTROPHORESIS
POLYOMA VIRUS, TRANSFORMED CELL LINES
IN VIVO, HAMSTER (0215)
BRYO
ANTIGEN, GASTRIC CANCER, MAN (0707)
CHICK, NEW AVIAN TUMOR VIRUS, HELPER
FACTOR (1086)
7,12-DIMETHYLBENZ(A)ANTHRACENE, DNA,
RNA, ACTINOMYCIN D, 1-MERCAPTO-1-
(BETA-4-PYRIDETHYL)BENZIMIDAZOLE
(1322)
IMPLANTATION, ULTRASTRUCTURE OF TERA-
TOMAS, MURINE TERATOMAS (1671)
KIDNEY, BENZO(A)PYRENE, MOUSE (2231)
DOCRINE GLAND
CARCINOMA (2173)*
PINEAL GLAND, 9,10-DIMETHYL-1,2-
BENZANTHRACENE, DEPIGMENTATION
RESPONSE, HAMSTER (0444)
TUMOR, PATHOGENESIS, ADRENAL CORTEX,
REVIEW (2161)
OMETRIUM
CANCER, CYTOLOGIC STUDY OF ASSOCIATION
HYPOESTROGENISM (1225)
CANCER, ISRAELI POPULATION, CERVICAL
CANCER (1175)
CANCER, SEX CHROMATIN, RADIATION
(0810)
CANCER, YOUNG WOMEN, PATHOGENESIS
(0747)*
CARCINOMA, EPIDEMIOLOGY, KENTUCKY
(2480)
CARCINOMA, FALLOPIAN TUBE, EPITHELIAL
HYPERPLASIA, ESTROGEN (1160)
CARCINOMA, FALLOPIAN TUBE HYPERPLASIA,
HUMAN (2027)
CARCINOMA, HYPERPLASIA (1282)
EPIDERMIZATION, MONKEY CERVIX, CHRONIC
ESTROGENIC STIMULATION (1158)
HYPERPLASIA, ADENOCARCINOMA, FERTILITY
(0743)
HYPERPLASIA, ADENOCARCINOMA,
SULFHYDRYL GROUPS, HUMAN (2468)
HYPERPLASIA, HORMONAL CONTRACEPTIVES,
SOMATIC EFFECTS, REVIEW (0871)*
HYPERPLASIA, INTRAUTERINE DEVICE (1706)
VIRUS, HERPESVIRUS (0622)
VIRONMENT
CARCINOGENS, INDUSTRY, ANIMAL FOOD,
AIR AND WATER (1747)

HUMAN MALIGNANCY, CHROMOSOMES, HAZARDS
(2101)
ENVIRONMENTAL HAZARD
AIRPLANE ENGINE SOOT, BENZO(A)PYRENE,
MOUSE (2228)
CANCER, EPIDEMIOLOGY, ITALY (1622)
CANCER INCIDENCE, CRACOW (1167)
CERVIX, HERPES-SIMPLEX TYPE-2 (0187)
CHEMICAL CARCINOGEN, GENETIC ACTION
(2168)*
COOPERATIVE RESEARCH EFFORT, CHEMICAL
CARCINOGENS (0377)*
CYTOCHROME P1-450, POLYCYCLIC 8YDRO-
CARBONS, MICROSOMES, RAT (1344)
HUMAN CANCER, FOOD ADDITIVES, PESTI-
CIDES (1275)
MUTATION, CHEMICAL MUTAGENS (0855)
NATURAL CARCINOGENS, SYMPOSIUM REVIEW
(1285)*
NEOPLASMS IN AQUATIC ANIMALS, BOTTOM
FEEDING FISH, OYSTERS, COMPARATIVE
ONCOLOGY (1273)
OCCUPATIONAL HAZARDS, ORGANIC AND
INORGANIC CARCINOGENS, REVIEW
(0877)*
SYNTHETIC SWEETENER, CYCLAMATE,
SACHARIN, CARCINOGENICITY, MAN,
REVIEW (2171)*
URBAN AREA, LUNG CANCER, EPIDEMIOLOGY
(2482)
ENZYME
ACETYLCHOLINESTERASE, NEUROBLASTOMA,
MOUSE (0783)
ACID AND ALKALINE NUCLEASE, BRAIN,
MALIGNANCIES (2080)
ACID AND ALKALINE PHOSPHATASE,
LACTIC AND GLUCOSE-6-PHOSPHATE
DEHYDROGENASE, LUNG (0127)
ACID DNASE, LEUKEMIA CELLS, CYTOTOXIC
EFFECT, MICE (1041)
ACID PHOSPHATASE, BETA-GLUCURONIDASE,
AFLATOXIN, LYSOSOMAL ENZYME ACTIVITY
(0916)
ACID PHOSPHATASE, MOUSE, CEREBRUM,
ASCITES (1684)
ACID PHOSPHATASE, X-IRRADIATION,
ULTRAVIOLET, MOUSE ENDOCRINE GLANDS
(2287)
ACID PHOSPHATASE ISOENZYME, RETICULUM
CELLS, LEUKEMIC RETICULOENDOTHELIO-
SIS (1637)
ACTIVITIES, RAUSCHER LEUKEMIA VIRUS
(1907)
ADENOSINE DEAMINASE ACTIVITY, PLATE-
LETS, CHRONIC MYELOID LEUKEMIA
(1643)
ADENYL CYCLASE, ADRENAL GLAND,
CARCINOMA, RAT (2537)
ADENYL CYCLASE, HEPATOMA, GROWTH RATE
(2498)
ALDOLASE ISOZYME ACTIVITY, NERVOUS
SYSTEM TUMORS (1255)
ALKALINE AND ACID NUCLEASES,
N-NITROSOMORPHOLINE, RAT LIVER
(2247)
ALKALINE PHOSPHATASE, LEUKOCYTES,
BENZENE, TOLUENE, OCCUPATIONAL
HAZARD (1374)*

ALKALINE PHOSPHATASE, REGAN ISOZYME, CANCER PATIENTS (2567)
 ALKALINE PHOSPHATASE, SUCCINIC DEHYDROGENASE, N-NITROSO-N-METHYL-URETHANE, LUNG HISTOLOGY, MOUSE (0486)
 ALKALINE PHOSPHATASE, THYMIC LYMPHOMA, MURINE LEUKEMIA VIRUS, RAT (0590)
 ALKALINE PHOSPHATASE ACTIVITY, SKELETAL NEOPLASMS (0327)
 AMINOPEPTIDASE ACTIVITY, MOUSE MAMMARY TUMOR VIRUS (1470)
 ARGINASE, ANAEROBIC GLYCOLYSIS, NEOPLASTIC CONVERSION (1143)
 ARGINASE, SV40, FIBROSARCOMA, LIVER, HAMSTER (1496)
 ARYL HYDROCARBON HYDROXYLASE, POLYCYCLIC HYDROCARBON, 17-BETA-ESTRADIOL, MOUSE (0891)
 ARYL HYDROCARBON HYDROXYLASE, SKIN, MOUSE, 9,10-DIMETHYLBENZANTHRACENE, 7,8-BENZOFLAVONE (0445)
 ARYL HYDROLASE, BENZO(A)PYRENE HYDROXYLATION, INHIBITION KINETICS, IN VITRO (0069)
 L-ASPARAGINASE, ANTIBODY, ASCITIC LEUKEMIA (1560)
 L-ASPARAGINASE, INHIBITION OF FOCUS-FORMATION, ROUS SARCOMA VIRUS, METHOTREXATE (1480)
 L-ASPARAGINASE, MITOTIC ACTIVITY IN LIVER CELLS, N-2-FLUORENYLACETAMIDE (1303)
 ASPARTYL TRANSCARBAMYLASE, RAUSCHER LEUKEMIA VIRUS, BLOOD, MOUSE (2321)
 AZO DYE REDUCTASE, LIVER, CECAL BACTERIA, RAT (0054)
 BENZO(A)PYRENE HYDROXYLASE, CARBON MONOXIDE, LIVER, RAT (0459)
 BENZO(A)PYRENE HYDROXYLASE, FLAVONE INDUCER, PULMONARY ADENOMA (0070)
 BENZO(A)PYRENE HYDROXYLASE, LUNG, HAMSTER (2230)
 BENZO(A)PYRENE HYDROXYLASE, 3-METHYLCHOLANTHRENE, PUROMYCIN, MICROSOMES (1805)
 BENZO(A)PYRENE HYDROXYLASE, 3-METHYLCHOLANTHRENE, RAT SKIN (0939)
 BENZO(A)PYRENE HYDROXYLASE, TOBACCO, PLACENTA (1799)
 CATALASE, LIVER TUMOR, ETHYL-ALPHA-P-CHLOROPHENOXYISOBUTYRATE (2114)
 CITRIC ACID CYCLE, LIVER, AFLATOXIN, MICE (0920)
 COLLAGENASE, CARCINOGENESIS, SKIN, MICE, DNA (1343)
 COLLAGENASE, MAMMARY CARCINOMA, INVASION ZONE, DNA (1649)
 CREATINE KINASE, CARBON TETRACHLORIDE, HEPATOCARCINOGENESIS, MOUSE (1288)
 CYSTEINE DESULFURASE, BETA-MERCAPTO-PYRUVATE DESULFURASE, CHROMOSOME MODALITY, HEPATOMA, RAT (0807)
 DAB-REDUCTASE, N,N-DIMETHYL-4-AMINO-AZOBENZENE, RAT LIVER (1315)
 DIETARY INDUCTION, HEPATOCARCINOGENS, 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE (0052)
 DIETARY INDUCTION, 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE, 2-METHYL-4-DIMETHYLAMINOAZOBENZENE (0051)
 DIHYDROFOLATE REDUCTASE, LYMPHOMA L1210 (1646)
 DIMETHYLNITROSAMINE DEMETHYLASE, 3-METHYLCHOLANTHRENE, CARBOHYDRATE REPRESSION (0474)
 DIMETHYLNITROSAMINE DEMETHYLASE, RAT LIVER, 3-METHYLCHOLANTHRENE (0466)
 DNA POLYMERASE, CHRONIC LYMPHOCYTIC LEUKEMIA, PLASMA (2082)
 DNA POLYMERASE, HELA, WI38 (2561)
 DNA POLYMERASE, HUMAN UROGENITAL TUMOR (0331)
 DNA POLYMERASE, MURINE LEUKEMIA, VIRUS (2320)
 DNA POLYMERASE, MYELOCYTOMATOSIS VIRUS, CHICK CELLS (1893)
 DNA POLYMERASE, RNA DEPENDENT, MOLONEY LEUKEMIA VIRUS, STREPTOVARICIN (1444)
 DNA POLYMERASE, ROUS SARCOMA VIRUS (0648)
 DNA POLYMERASE, VIRUS, MC29 TUMOR (1892)
 ENDONUCLEASE, KIDNEY CELL CULTURE, HAMSTER, POLYOMA VIRUS (0674)
 ENZYMATIC BLOCK, GANGLIOSIDE SYNTHESIS, DNA VIRUS-TRANSFORMED CELL LINES (0568)
 ESTERASE ACTIVITY, PLASMA, IRRADIATED RATS (1387)
 EXONUCLEASE, LIGASE, DNA, ROUS SARCOMA VIRUS (2368)
 GLUCOSE-6-PHOSPHATASE, HORMONE, LIVER, DIETHYLNITROSAMINE (1814)
 GLUCOSE-6-PHOSPHATE DEHYDROGENASE, A AND B TYPES, MULTIPLE CELL ORIGIN OF TUMOR, HEREDITARY NEUROFIBROMA (1687)
 GLUCOSE-6-PHOSPHATE DEHYDROGENASE ISOZYMES, LIVER, RHODAMINE SARCOMA RAT (0035)
 B-GLUCURONIDASE, CROTON OIL, RAT (2180)
 B-GLUCURONIDASE, DNA, BLADDER TUMORS HUMAN (2084)
 B-GLUCURONIDASE, PHENOLPHTHALEIN, CARCINOMA, MELANOMA, MOUSE (2085)
 GLUTAMATE, SUCCINATE, LACTATE, ISOCITRATE GLUCOSE-6-PHOSPHATE DEHYDROGENASES, SKIN, METHYLCHOLANTHRENE, MOUSE (0469)
 GLYCOGEN SYNTHETASE, GLYCOGEN, HEPATOMAS, RAT (2086)
 GLYCOLYSIS, OXIDATIVE, SV40, SIMIAN KIDNEY CELLS (1506)
 GLYCOLYTIC, HEPATOMA, RAT, TUMOR GROWTH (0739)
 GLYCOSYLTRANSFERASE ACTIVITY, POLYOM. BHK (1958)
 HEXOKINASE, HEPATIC TUMOR, GROWTH RAT (0288)
 HISTOCHEMISTRY, SHOPE PAPILOMA, VIRUS, RABBIT (2381)
 HYDROLYTIC, CARCINOMA OF COLON, FAMILIAL POLYPOSIS (0337)*

HYPOXANTHINE PHOSPHORIBOSYLTRANSFER-
 ASE, ADENINEPHOSPHORIBOSYLTRANSFER-
 ASE, LEUKOCYTES (2083)
 INDUCERS, URETHAN CARCINOGENESIS, MICE
 (2255)
 INDUCTION, BENZO(A)PYRENE, METABOLISM
 OF CARCINOGEN (1335)
 IODIDE PEROXIDASE, THYROID TUMOR,
 RAT (2557)
 ISOCITRATE DEHYDROGENASE, LACTATE
 DEHYDROGENASE, LYMPHOBLASTIC
 LEUKEMIA, SPLEEN, LIVER, 2URSA
 (1644)
 KREBS CYCLE, DIAPHORASES, PHOSPHATASES
 LIVER, DIETHYLNITROSAMINE, RAT (0960)
 LACTATE DEHYDROGENASE, CARCINOMA,
 PROSTATE, HAMSTER, HUMAN (2374)
 LACTATE DEHYDROGENASE, LEUKEMIA, VIRUS
 INTERFERON (1454)
 LACTATE DEHYDROGENASE, 6-PHOSPHO-
 GLUCONATE DEHYDROGENASE, PHOSPHO-
 HEXOSE ISOMERASE, BREAST CARCINOMA
 (0338)*
 LACTATE DEHYDROGENASE ISOENZYMES,
 PROSTATIC CANCER, SV40, HUMAN,
 HAMSTER (1508)
 LACTIC DEHYDROGENASE, EXPERIMENTAL
 TUMORS, CLASSIFICATION, MORPHOGENE-
 SIS (0966)
 LEUCINE AMINOPEPTIDASE ACTIVITY,
 DISSEMINATED MALIGNANT DISEASES
 (0788)
 LIVER, P-DIMETHYLAMINOAZOBENZENE, ACID
 PHOSPHATASE, ESTERASE, SUCCINIC
 DEHYDROGENASE (0922)
 LIVER, TRANSFER RNA, ETHIONINE (2146)
 LIVER ARGINASE, EHRlich ASCITES TUMOR,
 UREA CYCLE ENZYMES (2067)
 LYSOSOMAL, LIVER AND KIDNEY TISSUE,
 RENAL CARCINOMA (1645)
 LYSOSOMAL, MELANOMA, MOUSE (2542)
 LYSOSOMAL ACTIVITY, 4-DIMETHYLAMINO-
 AZOBENZENE, RAT LIVER LYSOSOMES
 (1784)
 LYSOSOMAL ACTIVITY, TUMOR GROWTH,
 MOUSE MELANOMA (1248)
 LYSOSOMAL CHANGES, LIVER, METASTASES,
 NON9ON9C SUR6ACTANTS (1680)
 LYSOZYME, RADIATION, COBALT 60, GAMMA
 IRRADIATION (2292)
 MAMMARY CELLS, HORMONES, RAT (2470)
 METHYLASE, BRAIN TUMORS, TRNA (2523)
 METHYLASE, CHROMATIN, HISTONE (2097)
 METHYLASE, DNA, TUMOR CELL CHROMATIN
 (2100)
 METHYLASE, TRANSFER RNA, CONTROL (2511)
 MICROBODY, MORRIS HEPATOMA (2545)
 MICROSOMAL DRUG-METABOLIZING ENZYMES,
 BILIARY EXCRETION, 3,4-BENZPYRENE
 (0458)
 MICROSOMAL ENZYME, ENVIRONMENTAL
 CONTAMINANTS (0848)
 MICROSOMAL HYDROXYLASE, 3,4-BENZ-
 PYRENE, AFLATOXIN B1 (0428)
 MURAMIDASE, POLYCYTHEMIA VERA,
 GRANULOCYTE (0320)
 NAD TETRAZOLIUM REDUCTASE, LDH,
 G6PDH, NERVOUS SYSTEM TUMORS (1196)

NEOPLASM PATHOGENESIS, MODIFICATION
 PROCESSES, REVIEW (0860)
 NONSPECIFIC ESTERASE, ACID PHOSPHA-
 TASE, MALIGNANT LYMPHOPROLIFERATIVE
 DISEASE (0257)
 NUCLEOSIDE DEAMINASE ACTIVITY, SPLEEN,
 FRIEND LEUKEMIA VIRUS, MOUSE (1901)
 ODONTOGENIC AMELOBLASTIC TUMORS,
 HISTOCHEMISTRY (0784)
 ORNITHINE DECARBOXYLASE, THIOACETAMIDE
 RNA METABOLISM (0039)
 ORNITHINE DECARBOXYLASE ACTIVITY,
 HEPATOMA, SARCOMA (0315)
 PATTERNS, HEPATOMA, DIFFERENT GROWTH
 RATE, MICE (2547)
 PEROXIDASE ACTIVITY, CHLOROMA, RAT
 (1650)
 PHENYLALANYL SYNTHETASE, PHENYLALANINE
 RNA (2521)
 PHOSPHATASE, MOUSE MAMMARY TUMORS,
 ENZYME DISTRIBUTION (1144)
 PHOSPHOFRUCTOKINASE, P-DIMETHYLAMINO-
 AZOBENZENE, RAT LIVER (1318)
 PHOSPHOGLUCOMUTASE ISOZYME, CHRONIC
 LYMPHATIC LEUKEMIA (0794)
 POLYMERASE, ENDONUCLEASE, RNA, DNA,
 ROUS SARCOMA VIRUS (0647)
 POLYMERASE, NUCLEIC ACID, ONCOGENIC
 VIRUS (0553)
 POLYMERASE, RNA, DNA, AVIAN MYELO-
 BLASTOSIS (0586)
 POLYMERASE, RNA, DNA, ROUS SARCOMA
 VIRUS (0651)
 PROTEASE, WHOLE BODY IRRADIATION,
 RABBIT (2274)
 PROTEASE INHIBITORS, TUMORIGENESIS
 PROMOTERS, 7,12-DIMETHYLBENZ(A)
 ANTHRACENE (0059)
 REVERSE TRANSCRIPTASE, HUMAN LEUKEMIA
 VIRUSES, VIRUS (0352)
 RIBONUCLEOTIDE REDUCTASE, CELL
 EXTRACT, NEOPLASTIC TISSUE, HUMAN
 (0781)
 RNA-DEPENDENT, DNA POLYMERASE, RNA
 VIRUS, ONCOGENIC VIRUS (0557)
 RNA POLYMERASE ACTIVITY,
 7,12-DIMETHYLBENZ(A)ANTHRACENE,
 MAMMARY GLAND CELL NUCLEI, RAT
 (1791)
 SERINE DEHYDRATASE, DIETHYLNITROSAMINE
 RAT (2427)
 SERINE HYDROXYMETHYL TRANSFERASE,
 LIVER, FRIEND VIRUS, MOUSE (2317)
 SERUM ALKALINE PHOSPHATASE, HODGKIN'S
 DISEASE, ISOZYMES (0246)
 SIALIC ACID TRANSFERASE, TRANSFORMED
 CELLS (1101)
 SORBITOL DEHYDROGENASE, DIETHYLNITRO-
 SAMINE CARCINOGENESIS, LIVER, RAT
 (0085)
 SUCCINIC DEHYDROGENASE, CYTOCHEMISTRY,
 AFLATOXIN B1, MUCOR HIEMALIS FUNGUS
 (1376)*
 SURVEY, REUBER MOUSE HEPATOMAS (2549)
 THYMIDINE KINASE, HERPES SIMPLEX,
 ULTRAVIOLET (2336)
 THYMIDINE KINASE, KIDNEY CELL, SV40
 VIRUS, HAMSTER (0667)

THYMIDINE KINASE, SV40, DNA SYNTHESIS,
 PARVOVIRUS H-1 (0210)
 THYMIDINE KINASE, YADA VIRUS, TUMORS
 (1429)
 TRANSFER RNA METHYLASE, NEOPLASTIC
 HAMSTER TISSUES (2088)
 TRANSFER RNA METHYLASE, VIRUS-
 TRANSFORMED CELLS (1950)
 TRANSFER RNA METHYLASE ACTIVITY,
 CHRONIC LYMPHOCYTIC LEUKEMIA,
 PHYTOHEMAGGLUTININ (2091)
 TRANSFER RNA METHYLASE ACTIVITY,
 GROWTH AND DIFFERENTIATION, NORMAL
 AND NEOPLASTIC TISSUE SYSTEMS (0791)
 TRNA METHYLASE, ACTIVITY, ADENO-
 VIRUS-12, HAMSTER (1049)
 TRNA METHYLASE, ASCITES TUMOR, MOUSE
 (2509)
 TRNA METHYLASE, 1,2-DIMETHYLHYDRAZINE,
 COLONIC TUMOR, MOUSE (2216)
 TRNA METHYLASE, MALIGNANCY (2474)
 TRNA METHYLASE, MORRIS HEPATOMAS
 (2512)
 TRNA METHYLASE, POLYOMA VIRUS (0217)
 TRYPTOPHANYL TRANSFER RNA SYNTHETASE,
 LYMPHOCYTIC LEUKEMIA, HUMAN (2510)
 TUMOR ISOENZYMES, 7,12-DIMETHYLBENZ-
 (A)ANTHRACENE, OOPHORECTOMY, RAT
 (2222)
 TYROSINASE, MELANOMA, MURINE (2541)
 TYROSINE AMINOTRANSFERASE,
 5-BROMODEOXYURIDINE, RAT HEPATOMA
 CELLS (2078)
 TYROSINE HYDROXYLASE, CELL-FREE
 EXTRACT, NEUROBLASTOMA (0567)
 TYROSINE HYDROXYLASE ACTIVITY, DOPA,
 HAMSTER ISLET CELL TUMORS (1222)
 TYROSINE HYDROXYLASE ACTIVITY,
 INHIBITION, HUMAN NEUROBLASTOMA
 (2064)
 TYROSINE TRANSAMINASE, CYCLOHEXIMIDE,
 PUROMYCIN, HEPATOMA (2551)
 EPENDYMOMA
 AVIAN ADENOVIRUS, CHICKEN-EMBRYO
 LETHAL-ORPHAN (0182)
 MORPHOLOGY, POLYGONAL CRYSTALLINE
 STRUCTURE (0249)
 EPIDEMIOLOGY
 ACUTE LYMPHOCYTIC LEUKEMIA, CHILDHOOD
 LEUKEMIA (1603)
 AMERICAN NEGROES, INCIDENCE OF
 BRONCHOGENIC CANCER (1623)
 BAVARIA, LEUKEMIA MORTALITY (0270)
 BEDOUINS IN ISRAEL, LIVER CANCER (1168)
 BENZENE EXPOSURE, LEUKEMIA (0121)*
 BREAST CANCER, HUMAN, CANINE (0277)
 BREAST CANCER RISK, AGE AT FIRST BIRTH
 (1187)
 BRONCHOGENIC CARCINOMA, AIR POLLUTION,
 CZECHOSLOVAKIA (0768)*
 CANCER, BREAST, GENITAL ORGANS,
 FEMALE, QUEBEC (0298)*
 CANCER, CHILD, CANADA (0755)
 CANCER, CHILDREN, ITALY (2055)*
 CANCER, CONNECTICUT, CIGARETTE SMOKING
 (1611)
 CANCER, CRACOW, URBAN AND COUNTRY,
 ENVIRONMENT (1167)

CANCER, ENVIRONMENTAL FACTORS, BERG
 ITALY (1622)
 CANCER, GASTROINTESTINAL TRACT, IN
 (2487)
 CANCER, GERIATRIC PATIENTS, REVIEW
 (0869)*
 CANCER, IRAN (2488)
 CANCER, KURGAN (0754)
 CANCER, MEXICO (1193)*, (1194)*,
 (1195)*
 CANCER, NORWAY (1190)*
 CANCER, QUEBEC (0767)*
 CANCER, REVIEW (0873)*
 CANCER, SUBSAHARAL AFRICA (1608)
 CANCER INCIDENCE IN AFRICA,
 ETIOLOGICAL ASSOCIATIONS (2040)
 CANCER MORTALITY, INCIDENCE, GERMA
 (2053)*
 CANCER MORTALITY, REGIONAL TEMPERA
 VARIATION (1617)
 CANCER MORTALITY, STATISTICAL
 COMPILATION, UN9T5D STATES (1602)
 CARCINOGENIC FACTORS, ECOLOGY, REV
 (0384)*
 CARCINOMA OF THE COLON, EASTERN AN
 WESTERN NATIONS, INTESTINAL BACT
 (1189)
 CERVICAL ATYPIA, COMPUTERIZED STUD
 (2045)
 CERVICAL CANCER, CANADA, PRECLINIC
 STAGE DETECTION, REVIEW (0368)
 CERVICAL CANCER, RISK IN PAROUS IN
 WOMEN (2042)
 CHILDHOOD CANCER, WILM'S TUMOR,
 CLINICAL FEATURES (1180)
 CHILDHOOD CANCER INCIDENCE, CANCER
 MORTALITY, ATOMIC BOMB IRRADIATI
 (0540)
 CHILDREN, THYROID CARCINOMA (1173)
 CHILE, RAINFALL, ESOPHAGEAL CANCER
 INCIDENCE (2037)
 CHINESE-BORN POPULATION OF SINGAPO
 LIVER CANCER (1165)
 CONNECTICUT, LIP CANCER (1612)
 CYTOLOGIC SCREENING, CERVICAL CANC
 MORTALITY (0297)*
 CZECHOSLOVAKIA, ORAL CAVITY (2484)
 DEATH RATES, HEMATOPOIETIC CANCER,
 OKLAHOMA (0761)
 DIAGNOSIS, MALIGNANT MELANOMA (163)
 ENGLISH CHILDREN, AFRICAN CHILDREN
 HODGKIN'S DISEASE (1607)
 ESOPHAGEAL CANCER, KAZAKHSTAN (076)
 GALLBLADDER CANCER, WORLD INCIDENC
 ETIOLOGY (0018)*
 GASTRIC CARCINOMA, GERMANY, DETECT
 MORTALITY (0765)*
 GENETIC AND ENVIRONMENTAL CLUSTERS
 HUMAN AND BOVINE LYMPHOSARCOMA,
 FAMILIAL CLUSTERS (2096)
 GEOGRAPHIC DIFFERENCES, HISTOLOGIC
 ORIGIN OF CANCER (0858)
 HODGKIN'S DISEASE, GERMANY (0272)
 HODGKIN'S DISEASE, JAPAN (0271)
 IMMIGRANT POPULATIONS, CANCER SITE
 (0857)
 INCIDENCE, AGE-ADJUSTMENT, FINLAND
 (0264)

DIA, CANCER INCIDENCE, BUCCO-
 PHARYNGEAL, CERVICAL (2038)
 AN, DISTRIBUTION OF CANCER, AFFECTED
 SITE (1179)
 RAEI POPULATION, ENDOMETRIAL AND
 CERVICAL CANCER (1175)
 WISH POPULATION, POLYCYTHEMIA VERA,
 INCREASED RISK OF MALIGNANCY (1615)
 REA, MALIGNANT NEOPLASMS (2054)*
 UKEMIA, CNS, CHILDREN, INCREASE
 (0283)
 UKEMIA, KENYA (1166)
 UKEMIA, SEX MORTALITY RATIO (0275)
 NG CANCER, AIR POLLUTION (0016)
 NG CANCER, INDUSTRIAL ENVIRONMENT
 (2482)
 NG CANCER, TOBACCO (1741)
 NG CANCER MORTALITY, AIR POLLUTION,
 AUSTRALIAN IMMIGRANTS (2049)
 MPHOGNULOMATOSIS, CHILDREN,
 BULGARIA (2483)
 MPHOGNULOMATOSIS, POLAND (1629)*
 MPHOSARCOMA, LEUKEMIA, DOGS (2039)
 SOTHELIOMA, PLEURA, ASBESTOS (2481)
 XICAN POPULATION IN TEXAS, GALL-
 BLADDER CANCER, DIET (1171)
 CROEPIDEMICS, VIRAL ONCOGENESIS IN
 MAN (1267)
 SSOURI, ANNUAL CANCER FREQUENCIES
 (1181)
 RTALITY RATES, CANCER OF THE
 PANCREAS, CIGARETTE SMOKING (1178)
 RTALITY RATES, CHILE, ESOPHAGEAL AND
 GASTRIC CANCER (1169)
 RTALITY RATES, TESTICULAR TUMOR,
 MAN, TREATMENT (1186)
 ULTIPL PRIMARY TUMORS, MAMMARY
 CANCER, FEMALE REPRODUCTIVE ORGANS
 (1621)
 OPLASTIC DISEASES, REVIEW (0868)*
 EW MEXICO INDIANS, BILE DUCT CANCER,
 GALLBLADDER CANCER (1616)
 ON-AFRICAN UGANDANS, AFRICAN UGANDANS
 TUMOR INCIDENCE (1609)
 ON-WHITE AMERICANS, AMERICAN MORTAL-
 ITY DISTRIBUTION, ESOPHAGEAL CANCER
 (1181)
 CCUPATIONAL EXPOSURE, NICKEL,
 COBALT, LUNG CANCER (1185)
 ARENTAL CANCER MORTALITY, SERUM
 CHOLESTEROL AMONG OFFSPRING (1625)
 ATHOLOGY, BLADDER CARCINOMA, REVIEW
 (0380)*
 ATHOLOGY, OSTEOPENIC SARCOMA (0752)
 OLAND, PULMONARY CANCER (1192)*
 RIMARY LUNG CANCER, ALESSANDRIA
 (1184)
 ULMONARY CANCER INCIDENCE, SARDINIA,
 TUMOR MORBIDITY DATA (0766)*
 ALIVARY GLAND TUMORS, EASTERN
 GERMANY, MALIGNOMAS, POLYMORPHIC
 ADENOMAS (0285)
 MOKING, CARCINOMA OF THE TONGUE
 (0847)
 OUTHERN IRAN, SKIN CANCER INCIDENCE
 (2041)
 OY BEAN PASTE, KOREA, STOMACH CANCER
 (1174)

SPACE-TIME CLUSTERING, LEUKEMIA,
 CHILDREN (0278)
 SUGAR AND FAT INTAKE, BREAST CANCER,
 BLOOD GROUP A (0265)
 SWEDEN, CHORIOCARCINOMA, HYDATIDIFORM
 MOLE (0753)
 TUMOR, AGE, REVIEW (1725)
 TUMOR, QUEBEC (1631)*
 TUMOR, SMOKING, TUNISIA (1628)*
 UNITED STATES, OVARIAN CANCER, UTERINE
 CANCER (1619)
 UTAH, SURVIVAL RATE, MELANOMA (1614)
 WEST GERMAN ARMY, LEUKEMIA (1613)
 EPIDERMIS
 BIOELECTROMETRIC MEASUREMENT,
 3-METHYLCHOLANTHRENE, MOUSE (0075)
 EPIDERMIZATION, 3-METHYLCHOLANTHRENE,
 UTERUS, MICE (1804)
 HYDROCORTISONE, CHALONE, DNA SYNTHESIS,
 MOUSE (2059)
 MALIGNANT FIBROBLASTS, DIFFERENTIATION
 FACTOR (2075)
 ULTRASTRUCTURAL STUDY, SUNLIGHT
 EXPOSURE, HUMAN (1855)
 UKEA-EXTRACTABLE ANTIGENS, BENIGN AND
 MALIGNANT TUMORS, MOUSE (0726)
 EPIDIDYMUS
 ADENOMATOID TUMOR, MESOTHELIAL ORIGIN,
 ULTRASTRUCTURE (1161)
 EPIGENESIS
 NEOPLASTIC TRANSFORMATION, EMBRYONIC
 SYSTEMS, REVIEW (0392)*
 EPIPHARYNX
 EPITHELIAL CARCINOMA, RETICULAR CELL
 SARCOMA, REVIEW (0013)
 EPITHELIOMA
 ARSENIC, BOWEN'S DISEASE, HUMANS
 (1368)
 INVASION, XIPHISTERNAL CARTILAGE (0250)
 MAMMARY GLAND, CHRONIC CYSTIC MASTITIS
 MALIGNANT TRANSFORMATION (1159)
 SMALLPOX VACCINE SCARS, MAN (0339)*
 EPITHELIUM
 CARCINOMA, RETICULAR CELL SARCOMA,
 EPIPHARYNGEAL CANCER (0013)
 CERVIX UTERI, MORPHOLOGY, CARCINOGENESIS,
 HUMAN (0853)
 MOUSE DUODENUM, GAMMA-IRRADIATION,
 CELL PRODUCTION (0123)
 MOUSE KIDNEY, CELL DENSITY, PRO-
 LIFERATION (0813)
 OROPHARYNGEAL TUMOR, FACIAL TUMOR,
 MOUSE, N-NITROSOPENTAMETHYLENEIMINE,
 N-NITROSOHEXAMETHYLENEIMINE (0479)
 TRACHEA, MORPHOLOGY, VITAMIN A
 DEFICIENCY, METAPLASIA, RAT (1209)
 ERGOCORNINE
 2-BR-ALPHA-ERGOKRYPTIN, MAMMARY
 HYPERPLASTIC NODULES, PROLACTIN,
 MICE (0312)
 2-BROMO-ALPHA-ERGOCRYPTINE, MAMMARY
 HYPERPLASTIC NODULE (1207)
 ERYTHROCYTE
 ADENOVIRUS TYPE 7, VIRAL ADSORPTION
 (0614)
 MOUSE MAMMARY TUMOR VIRUS, DNA (2345)
 OSMOTIC FRAGILITY, FRIEND LEUKEMIA
 VIRUS (1033)

ROLE, PHYTOHEMAGGLUTININ-STIMULATED
 HUMAN LYMPHOCYTES (1571)
 VIRUS CARRIER, FRIEND, RAUSCHER, MICE
 (2322)
 ERYTHROPOIETIN
 3-METHYLCHOLANTHRENE, SKIN TUMOR,
 MOUSE (2233)
 ESOPHAGUS
 ACHALASIA, CARCINOMA, HUMAN (1700)
 CANCER, FAMILIAL INCIDENCE, EPIDEMI-
 OLOGY, KAZAKHSTAN (0760)
 CANCER, GASTRIC SURGERY, RECTAL CANCER
 (1228)
 CANCER, NON-WHITE AMERICANS, AMERICAN
 MORTALITY DISTRIBUTION (1181)
 CANCER INCIDENCE, CHILE, RAINFALL
 (2037)
 CARCINOMA, CAUSTIC ULCERATION, MAN
 (0988)*
 CARCINOMA, TYLOSIS, GENETIC LINKAGE
 (0776)
 EPITHELIOMA, CAUSTIC STENOSIS, MAN
 (1154)
 PRECANCEROUS STATES, CICATRITION,
 PEPTIC STENOSIS, SURGERY (0851)
 ESTRADIOL
 ADRENOCORTICAL CARCINOMA, RAT (0890)
 CASTRATION, THYROID, EPIDERMOID CYST,
 RAT (0416)
 17-BETA-ESTRADIOL
 ARYL HYDROCARBON HYDROXYLASE, POLY-
 CYCLIC HYDROCARBONS, MOUSE (0891)
 ESTROGEN
 CARCINOMA, RNA AND DNA METABOLISM
 (1770)
 CHANGES IN RAT UTERUS, INTRAUTERINE
 CONTRACEPTIVE DEVICE (0985)
 DIETHYLSTILBERTROL, ESTRADIOL, CHANGES
 IN CERVICAL EPITHELIUM, MONKEYS
 (1769)
 GROWTH OF TUMOR, ESTROGEN-DEPENDENT
 MAMMARY TUMOR (1993)
 MAMMARY CARCINOGENESIS, X-IRRADIATION
 (1295)
 PHOSVITIN, SERYL TRNA, METAZOAN (2475)
 TUMOR, HORMONE RESPONSIVENESS, BINDING
 (0834)
 ETHIONINE
 S-ETHYL-L-CYSTEINE, CARCINOGENICITY,
 PHOSPHORYLATION, MOLECULAR STRUCTURE
 SPECIFICITY, LIVER, RAT (2192)
 NODULES, LIVER, ULTRASTRUCTURE (1296)
 TRANSFER RNA, ENZYMES, LIVER (2146)
 DL-ETHIONINE
 HYPERPLASTIC NODULE, RAT LIVER (0430)
 ETHYL METHANESULFONATE
 METABOLISM, MOUSE (0902)
 URETHAN, MEIOTIC ABNORMALITIES (1828)
 N-ETHYL-N'-NITRO-N-NITROSOGUANIDINE
 SKIN, MOUSE (2253)
 ETHYL-NITROSOUREA
 CANCER, TRANSPLACENTAL CARCINOMA,
 RATS (0478)
 DNA, LIVER (0427)
 NEUROGENIC MALIGNANCIES (0090)
 TRANSPLACENTAL, BRAIN TUMORS (0964)
 4-ETHYLSULFONYLNAPHTHALENE-1-SULFONAMIDE
 MOUSE, BLADDER, EPITHELIUM (1300)

ETIOLOGY
 BRONCHIAL CARCINOMA, REVIEW (0872)
 CANCER, REVIEW (0883)*
 NONGONADAL NEOPLASM, TURNER'S SYND
 (0012)
 SKIN CANCER, CHRONIC LYMPHOCYTIC
 LEUKEMIA (0318)
 EWING'S TUMOR
 ORIGIN OF TUMOR, GROWTH PATTERN OF
 TUMOR IN VITRO (1704)
 EYE
 CARCINOMA IN CATTLE, HIGH-VOLUME
 FEEDING (0780)
 CONJUNCTIVAL LESIONS, AFRICAN PATI
 PINGUECULA (1213)
 ORBITAL TUMOR, EPIDEMIOLOGY, UGANDA
 (2492)
 RETINOBLASTOMA, BLOOD (1666)
 EYELID
 BASAL CELL CARCINOMA (0274)
 FACE
 LIP, RADIATION THERAPY, MELANOMA
 (0547)
 FACTOR
 RENAL INFLUENCE ON SERUM TITER, BO
 MARROW COLONY-STIMULATING FACTOR
 MICE (0332)
 FALLOPIAN TUBE
 EPITHELIAL HYPERPLASIA, ENDOMETRIAL
 CARCINOMA, ESTROGEN (1160)
 HYPERPLASIA, ENDOMETRIAL CARCINOMA
 HUMAN (2027)
 FAMILIAL POLYPOSIS
 COLON, CARCINOMA OF THE RECTUM,
 HEREDITARY DISTRIBUTION (1245)
 COLON, DESMOID TUMORS (1156)
 HYDROLYTIC ENZYME DISTRIBUTION,
 CARCINOMA OF COLON (0337)*
 FANCONI'S ANEMIA
 CHROMOSOME ABERRATIONS, CHROMATID
 ABNORMALITIES (1220)
 MYELOMONOCYTIC LEUKEMIA, CHROMOSOM
 VIRUS (0150)
 FEMUR
 MEDULLARY CANAL, 90S GAMMA, 90Y,
 DOSIMETRY, RAT (1405)*
 BETA-RADIATION, EXPERIMENTAL OSTEO
 SARCOMA, RAT (0543)
 FERRIDEXTRAN SPOFA
 SARCOMA, ANTIGENICITY, RAT (0900)
 SARCOMA, TUMOR TRANSPLANTABILITY,
 KARYOTYPE (0706)
 FERRITIN
 ASBESTOS, MESOTHELIOMA, HUMAN (225
 HEPATOMA, RAT (2550)
 RIBOSOMAL, RAT LIVER, CARCINOGENS
 (0475)
 FERTILITY
 ENDOMETRIAL HYPERPLASIA, ADENO-
 CARCINOMA (0743)
 FIBROBLAST
 DIFFUSION CHAMBER, SPONTANEOUS
 MALIGNANT TRANSFORMATION, MURINE
 (1584)
 EMBRYONIC HUMAN FIBROBLAST, POLYOM
 VIRUS, ROUS SARCOMA VIRUS, SENDA
 VIRUS (0675)
 LIVER, VIRUS PART9CLES (1413)

LUNG, SV40, SUSCEPTIBILITY (1490)
 RIBOSOMAL RNA, ACTINOMYCIN D (1659)
 SV40, POLYOMA VIRUS, GLYCOLIPIDS (1102)
 VIRUS TRANSFORMED, DENSITY INHIBITION, MOUSE (1500)

IBROMA
 ESTROGENS, POLYETHYLENE STRIPS, UTERINE TUBES, GUINEA PIG (0815)
 GERBIL CELL LINE, INTRACISTERNAL TYPE A PARTICLES (1869)

IBROSARCOMA
 ALPHA PARTICLE IRRADIATION, RAT (0992)
 AT-TYPE, GC-TYPE ADENOCARCINOMA, POLYOMA VIRUS, DNA (0220)
 BENZ(A)PYRENE, RNA, IMMUNOREACTIVITY (0222)
 INDUCTION, X-IRRADIATION, HUMAN (1849)
 3-METHYLCHOLANTHRENE, BENZO(A)PYRENE, PROSIMIANS (0073)
 SMALLPOX VACCINATION (1416)

IBROSIS
 SUBMUCOUS, PRECANCEROUS CONDITION, SQUAMOUS CELL CARCINOMA (0247)

LAVONE
 PULMONARY ADENOMA, BENZO(A)PYRENE HYDROXYLASE ACTIVITY (0070)

-2-FLUORENYLACETAMIDE
 L-ASPARAGINASE, MITOTIC ACTIVITY IN LIVER CELLS (1303)
 CARCINOGEN-INHIBITOR, ACETOTOLUIDIDE ISOMERS, AMINOBENZIC ACID (0041)
 CYCLOPHOSPHAMIDE, BLADDER CARCINOMAS (1302)
 CYCLOPHOSPHAMIDE, ESTABLISHED CELL LINES, URINARY BLADDER CARCINOMA (1304)
 LIVER CARCINOGENESIS, HYPERPLASTIC HEPATIC NODULES (1299)
 LIVER PLASMA MEMBRANES, LIPID COMPOSITION (1305)
 POLYNUCLEOTIDE, FLUORENYLAMINE, RNA, DNA (1306)

-FLUORENYLACETAMIDE
 HYPERPLASTIC NODULE, RAT LIVER (0430)
 TRNA, BINDING, RAT LIVER (1773)

-N-2,7-FLUORENYLENEBISACETAMIDE
 HEPATOMA, X-IRRADIATION, ACCELERATED INDUCTION (0040)

-1-BIS(4-FLUOROPHENYL)-2-PROPYNYL N-CYCLOHEPTYLCARBAMATE
 MALIGNANT LYMPHOMA, RAT (1287)

-1-BIS(4-FLUOROPHENYL)-2-PROPYNYL N-CYCLOOCTYLCARBAMATE
 MALIGNANT LYMPHOMA, RAT (1287)

OLIC ACID
 CARCINOGENIC METAL CHELATES (1292)
 UPTAKE, PHYTOHEMAGGLUTININ, HUMAN LYMPHOCYTES (0701)

OOD
 ADDITIVES, CARCINOGENICITY, REVIEW (2176)*

ORMIC ACID 2-(4-(5-NITRO-2-FURYL)-2-THIAZOLYL) HYDRAZIDE
 RENAL CARCINOMAS (0037)

REUND ADJUVANT
 BERGOLZ VIRUS, RETICULOSARCOMATOSIS, MOUSE (1477)

CHEMICAL CARCINOGENS, CHROMOSOMAL ALTERATION, PLASMA CELL TUMOR (0102)
 GRANULOMA, CARRAGEENAN (0103)
 3-METHYLCHOLANTHRENE, IMMUNOLOGICAL PROCESSES, RAT (2232)
 PLASMA CELL TUMOR, MICE (0395)
 PLASMACYTOMA, MICE (0394)
 RAUSCHER VIRUS, LEUKEMIA, MOUSE (2323)
 THYMUS, LUNGS, CELL PROLIFERATION, GUINEA PIG (1307)
 TUMOR TRANSPLANTATION, METASTASES, RAT (2022)*

FURAZOLIUM
 COUMARINS, AFLATOXINS, GUINEA PIG, HYPERSENSITIVITY (0424)

GADOLINIUM
 CARCINOGENESIS, YTTERBIUM (0403)

GALLBLADDER
 CANCER, MEXICAN POPULATION IN TEXAS, DIETARY ETIOLOGY (1171)
 CANCER, NEW MEXICO INDIANS, BILE DUCT (1616)
 CARCINOMA, CHOLESTEROL, DIMETHYL-NITROSAMINE, HAMSTER (1347)
 URINARY TRACT, N-(4-(5-NITRO-2-FURYL)-2-THIAZOLYL)FORMAMIDE, N-(4-(5-NITRO-2-THIAZOLYL)ACETAMIDE, CARCINOGENICITY (0038)

GANGLIONEUROMA
 NEUROBLASTOMA, TURNER'S SYNDROME, NONGONADAL NEOPLASIA (0012)
 RAT ADRENAL MEDULLA, PREOPTIC-ANTERIOR HYPOTHALAMIC LESION (1259)

GANGLIOSIDE
 ALTERATION, SV40, POLYOMA VIRUS (1091)
 SYNTHESIS, DNA VIRUS-TRANSFORMED CELL LINES, ENZYMATIC BLOCK (0568)

GASTROINTESTINAL TRACT
 ANO-RECTAL FISTULA, MALIGNANT TRANSFORMATION, CARCINOMA (0341)*
 CANCER, EPIDEMIOLOGY, INDIA (2487)
 DMBA, PENETRATION-FIXATION, MESENTERIC TUMORS (0926)
 ESOPHAGEAL AND GASTRIC CANCER, CHILE, MORTALITY RATES (1169)
 GALLBLADDER CANCER, EPIDEMIOLOGY, ETIOLOGY (0018)*
 GASTRIC STUMP, PRIMARY CANCER, ULCER DISEASE GASTRECTOMY, MAN (0140)*
 HUMAN FETAL GUT ANTIGEN, MALIGNANCIES, DETECTION OF ANTIGEN (1566)
 LUNG, BENZO(A)PYRENE, 3,4-BENZFLUORANTHENE, CARCINOMA TISSUE (0912)
 PAPILLOMA, CARCINOMA, NITROSAMINE (0476)
 SCHWANN CELLS, NEURINOMA, PATHOGENESIS FIBROCYTES (1593)
 TRANSPLACENTAL INDUCTION, RATS, ETHYL NITROSUREA (0478)
 TUMOR, CHROMOSOME (2586)*

GENETICS
 ADMIXTURE, CANCER, NEGRO (2094)
 AUTOSOMAL DOMINANT INHERITANCE, CONGENITAL CANCER, REVIEW (1278)
 CARCINOMA OF THE ESOPHAGUS, TYLOSIS (0776)
 CARCINOMA OF THE RECTUM, FAMILIAL POLYPOSIS OF THE COLON (1245)

CONGENITAL TUMOR, IMMUNITY, ACTIVE,
 ADOPTIVE (1547)
 CYTOGENIC ABNORMALITY, AFFECTED
 SIBLINGS, LYMPHOSARCOMA (0694)
 DIZYGOTIC TWINS, MONOZYGOTIC TWINS,
 TUMOR DEVELOPMENT (0861)
 ENVIRONMENT, CHEMICAL CARCINOGEN
 (2168)*
 ESOPHAGUS, FAMILIAL INCIDENCE,
 EPIDEMIOLOGY, KAZAKHSTAN (0760)
 FAMILIAL AGGREGATION, ACUTE LYMPHO-
 CYTIC LEUKEMIA (0796)
 FAMILIAL LEUKEMIA, HUMAN AND BOVINE
 LYMPHOSARCOMA, CLUSTERS (2096)
 FAMILIAL OCCURRENCE, CAROTID BODY
 TUMORS, BILATERAL TUMOR (1258)
 FAMILIAL POLYPOSIS, POLYPOID LYMPHOID
 HYPERPLASIA, TERMINAL ILEUM (0827)*
 FAMILIAL VON HIPPEL-LINDAU'S DISEASE,
 PHEOCHROMOCYTOMA (0828)*
 FORWARD MUTATIONS, 8-AZAGUANINE
 SENSITIVITY, X-IRRADIATION (1393)
 HEREDITARY NEUROFIBROMA, DOUBLE
 ENZYME PHENOTYPE, MULTIPLE CELL
 ORIGIN OF TUMOR (1687)
 HYBRIDIZATION, KARYOLOGIC CHARACTER-
 ISTICS, MICE (0838)
 HYBRIDIZATION, NUCLEAR DNA, BACTERIAL
 DNA, TUMOR TISSUE (1254)
 LETHAL YELLOW GENE, RAT RETICULAR
 TUMOR DEVELOPMENT (1198)
 LEUKEMIA, DERMATOGLYPHIC PATTERNS
 (0363)
 LYMPHOSARCOMA, RABBIT (0802)
 MENINGEOMA, FAMILIAL, INTRACRANIAL
 (1262)
 MITOTIC CONVERSIONS, YEAST CELLS,
 AROMATIC AMINES (0412)
 MOSAICISM, OVARIAN TUMOR, GONADOBLAS-
 TOMA (1689)
 MUTATION (2177)*
 NEOPLASIA, FANCONI'S ANEMIA, HUMAN
 (2534)
 PARENTAL CANCER MORTALITY, EPIDEMIOLO-
 GY, SERUM CHOLESTEROL (1625)
 PHENOTYPE, POLYOMA VIRUS (2385)
 PREDISPOSITION, CELTIC POPULATION,
 MALIGNANT MELANOMA (2093)
 PREDISPOSITION, PAPILLARY ADENO-
 CARCINOMA, FAMILIAL OVARIAN
 CARCINOMA (0808)
 SKIN HETEROGENIZING VIRUS, STRAIN
 SPECIFIC VIRUS (0145)
 SOLID TUMOR, LEUKEMIA, INCIDENCE IN
 TWINS, MORTALITY (1606)
 STRAIN DIFFERENCES, IMMUNOPATHOLOGICAL
 PROFILE, TUMOR PROFILE, REVIEW
 (0393)*
 SUSCEPTIBILITY, THYMIC LYMPHOMA, CELL-
 FREE THYMIC SUPERNATANT (0594)
 SUSCEPTIBILITY TO LEUKEMIA INDUCTION,
 AKR THYMUS GRAFT, GROSS VIRUS
 (0172)
 SUSCEPTIBILITY TRANSMISSION, MAMMARY
 TUMOR VIRUS, MILK TRANSMISSION
 (0631)
 TRANSMISSION, MOUSE MAMMARY TUMOR
 VIRUS (0627)
 TWIN, CANCER INCIDENCE (0365)
 TWIN, LEUKEMIA, REVIEW (0364)
 TWIN METHOD, CANCER INCIDENCE, SMOKI
 (0500)
 TWIN PAIR, SMOKING, LUNG CANCER
 MORTALITY (0109)
 TWIN ZYGOSITY, CONCORDANCE DETERMINA-
 TION, NEOPLASTIC DISEASE (0826)*
 VIRAL, LETHAL MUTATION (0864)*
 VIRAL GENOME, ROUS SARCOMA VIRUS,
 HAMSTER CELLS (1486)
 WHITE-NEGRO ADMIXTURE, BREAST CANCER
 INCIDENCE (1699)
 GLIOBLASTOMA
 ASTROCYTOMA, N-NITROSOMETHYLUREA, RA
 (1991)
 GLIOMA
 ASTROCYTOMAS, N-NITROSAOMETHYLUREA,
 RAT (1821)
 BRAIN, PROTEIN S100 (1567)
 CANINE, ULTRASTRUCTURE, ROUS SARCOMA
 VIRUS (1484)
 CHROMOSOME, DOUBLE-MINUTES, HUMAN
 (1260)
 HETEROLOGOUS ANTIGLIOMA "CARRIER"
 ANTIBODIES, HUMAN (2018)
 TYPE C VIRUS, HUMAN (1018)
 GLOMUS
 TUMOR, ULTRASTRUCTURE, HISTOGENESIS
 (1227)
 GLUCOSE
 ENHANCED UPTAKE, PSEUDOTYPE SARCOMA
 VIRUS, HAMSTER (2354)
 METABOLISM, CANCER BIOCHEMISTRY,
 REVIEW (0007)
 GLYCINE DERIVATIVES
 N-DIAZOACETYLGLYCINAMIDE,
 N-DIAZOACETYLGLYCINE HYDRAZIDE,
 CARCINOGENICITY, MOUSE (0401)
 GLYCOGEN
 GRANULES, HUMAN MENINGOTHELIAL
 MENINGIOMAS (2104)
 GLYCOLYSIS
 HEPATOMA, RAT, TUMOR GROWTH (0739)
 GLYCOPROTEIN
 CANDIDA ALBICANS, 3-METHYLCHOLANTHRE
 COCARCINOGEN, RODENT (1801)
 GRANULOCYTE
 KINETIC STUDY, ACUTE MYELOMONOCYTIC
 LEUKEMIA, ACUTE MYELOGENOUS
 LEUKEMIA (0290)
 POLYCYTHEMIA VERA, MURAMIDASE (0320)
 GRANULOMA
 CARRAGEENAN, FREUND'S ADJUVANT (0103)
 PLASMA CELL, MINERAL OIL TUMOR INDUC-
 TION, VIRUS-LIKE PARTICLES (0396)
 GROWTH
 ALTERATION OF VIRUS IN CULTURE,
 MURINE SARCOMA, FELINE LEUKEMIA
 (1934)
 ASCITES TUMOR, RADIATION, RAT (2496)
 ASCITIC LEUKEMIA, L-ASPAKAGINASE,
 ANTIBODY (1560)
 BEHAVIOR, MATRIX CULTURE, HUMAN
 BRAIN TUMOR (0303)*
 CARCINOGENESIS, NORMAL CELL DEVELOP-
 MENT, RNA DEPENDENT DNA SYNTHESIS
 (1268)

CARCINOMA, SKIN, CERVIX, NASOPHARYNX (1562)
 CELL CYCLE, HUMAN LEUKEMIA, TUMOR GROWTH KINETICS (1281)
 CHARACTERISTICS, 51CR-RBC DILUTION, ASCITIC PLASMACYTOMA (0291)
 CHICK EMBRYO, EHRLICH ASCITES CARCINOMA, METASTASES (2144)*
 CONTROL, PHOSPHATE, URIDINE, TRANSPORT INHIBITORS, 3T3 (1960)
 DIFFERENTIATION, NORMAL AND NEOPLASTIC TISSUE, TRANSFER RNA METHYLASE ACTIVITY (0791)
 DYNAMICS, WALKER'S CARCINOMA, GASTRIC WALL, RAT (0763)
 ENHANCEMENT, 3-METHYLCHOLANTHRENE, MURINE SARCOMA (1986)
 ENZYME ACTIVITY, MOUSE MELANOMA, LYSOSOMAL ENZYME ACTIVITY (1248)
 FACTOR, BONE MARROW, BLOOD FACTOR (0328)
 FACTOR, CHALONE, SQUAMOUS CELL CARCINOMA (1208), (1216)
 FELINE LEUKEMIA VIRUS, IN HUMAN CELLS (1895)
 HERPES SIMPLEX VIRUS, BURKITT'S LYMPHOMA CELLS (1923)
 INHIBITION, AGGLUTININ, POLYOMA VIRUS, CONCANAVALLIN A (0679)
 INHIBITION, WALKER 256 CARCINOSARCOMA, ZINC-DEFICIENT DIET (1232)
 INHIBITORS, LIVER, HEPATOMA, ARGINASE, RAT (2072)
 INTESTINAL TUMORS, 1,2-DIMETHYLHYDRAZINE, AUTORADIOGRAPHY (0044)
 INVASIVE TUMORS, ACID PHOSPHATASE, MOUSE, CEREBRUM (1684)
 KINETICS, TRANSFORMED CELLS, DEATH RATE (2052)
 LIVER, PARTIAL HEPATECTOMY, RATS (1350)
 MALIGNANCY, DIFFERENTIATION, HETERO-TOPIA (0379)*
 MALIGNANT FIBROBLASTS, EPIDERMIS, DIFFUSIBLE FACTOR, DIFFERENTIATION (2075)
 MORRIS HEPATOMA (2499)
 MORRIS HEPATOMA, STRUCTURE (2495)
 OVERGROWTH STIMULATING ACTIVITY, ROUS SARCOMA VIRUS, SONIC DISRUPTION OF CELLS (0644)
 PATTERN OF TUMOR IN VITRO, EWING'S TUMOR, ORIGIN (1704)
 PHASE, MALIGNANT TRANSFORMATION IN VITRO, METABOLIC CHANGES (0854)
 PHASE, VIRUS-TRANSFORMED CELLS, SURFACE GLYCOPROTEINS (1939)
 POLYOMA VIRUS, PROTEIN SYNTHESIS, DENSITY (1108)
 POLYOMA VIRUS, 3T3 AND BALB LINES, MITOSIS, MORPHOLOGY (0673)
 PROMOTING EFFECTS, ERlich SUBCUTANEOUS CARCINOMA, 5-N-METHYLATED LYSINE (0816)
 RATE, CANCER CELLS, METASTASES, PROLIFERATION, GOMPERTZIAN CURVE (1732)

RATE, HEXOKINASE, HEPATIC TUMOR (0288)
 RATE, MORRIS HEPATOMA, MINIMUM DEVIATION (0293)
 RATE, PAROTID GLAND TUMOR, 32P ACCUMULATION (1634)*
 RATE, TUMOR, RISK, BRONCHOGENIC CARCINOMA (1626)
 REGULATION, CELL, PROTEIN CONFORMATION SERUM (1673)
 REGULATION, POLYOMA-TRANSFORMED, MOUSE, HAMSTER (0350)
 REPLICATION OF VIRUS, FRIEND VIRUS, BACTERIAL ANTIGENS (1899)
 RETICULUM CELL SARCOMA, LYMPHOSARCOMA, LYMPH NODE (1236)
 SOLID HUMAN TUMORS, CELL CYCLE, AUTO-RADIOGRAPHIC ANALYSIS (0302)
 STIMULATION, FACTOR, ISOELECTRIC FOCUSING, HUMAN (2571)
 SV40, TRANSFORMATION, MOUSE CELLS (2370)
 TRANSFORMED CELLS, SV40, HERPES SIMPLEX (1493)
 TUMOR, PATHOGENESIS, SARCOMA (1729)
 TUMOR, PROMOTION, SODIUM COBALTNITRITE COBALT CHLORIDE (1339)
 TUMOR VASCULARIZATION, TUMOR ANGIO-GENESIS FACTOR (1647)
 HAIR
 7,12-DIMETHYLBENZ(A)ANTHRACENE, SUSCEPTIBILITY TO TUMOR INDUCTION, HAIRLESS MICE (0446)
 FOLLICLE, HISTOGENESIS, BASAL CELL EPITHELIOMA (0862)*
 FOLLICLE CYCLE, SKIN SUSCEPTIBILITY, 7,12-DIMETHYLBENZ(A)ANTHRACENE, MOUSE (0443)
 HAND
 SKIN OF ARM AND HAND, SQUAMOUS CELL CARCINOMA OF SKIN, SUNLIGHT (0997)
 HAPTEN
 IMMUNOGLOBULIN A, MYELOMA (2008)
 HEAD
 NECK, SQUAMOUS CELL, CARCINOMA, TOBACCO (0850)
 NECK TUMORS, CHILDREN, BURKITT'S LYMPHOMA (1188)
 HEART
 CARDIAC MYXOMA, ULTRASTRUCTURE OF LESION (1253)
 FIBROBLAST CELL CULTURE, ADENOVIRUS, RABBIT (0181)
 HEMAGGLUTINATION
 INHIBITOR ADENOVIRUS, SPECIFICITY (0183)
 HEMATOPOIESIS
 GAMMA-RAY, NEUTRON IRRADIATION (1380)
 PHYTOHEMAGGLUTININ-STIMULATED LYMPHOCYTES, HEME-SYNTHESIS (0700)
 RADIATION, MOUSE (2277)
 SPLEEN, FRIEND LEUKEMIA VIRUS, RADIATION (1898)
 TESTOSTERONE, RADIATION (1848)
 HEMOGLOBIN
 LEUKEMIA CELL, MURINE VIRUS (1897)
 HEPATOMA
 ASCITES, PERITONEAL FLUID, IMMUNITY, PASSIVE TRANSFER (1555)

CHEMOTACTIC AGENT, MICE (0300)
 CYSTEINE DESULFURASE, BETA-MERCAPTO-
 PYRUVATE DESULFURASE, CHROMOSOME
 MODALITY, RAT (0807)
 DIETHYLNITROSAMINE, ANTIGENICITY, RAT
 (0956)
 DIMETHYLAMINOAZOBENZENE, ANTIGENS,
 RAT (2423)
 DNA, GENE AMPLIFICATION, RAT (2212)
 ENZYME PATTERNS, DIFFERENT GROWTH
 RATE, MICE (2547)
 ALPHA-FETOPROTEIN, ISOLATION, HUMAN
 (1580)*
 GLYCOLYTIC ENZYMES, RAT, GROWTH (0739)
 HEPATECTOMY, HYPERTROPHY, RATS (2214)
 LYMPHOCYTES, MIGRATION INHIBITING
 FACTOR, GUINEA PIG (2440)
 MORRIS, EMBRYONIC IMPLANT, MINIMUM
 DEVIATION (0293)
 MORRIS, GROWTH (2499)
 MORRIS, GROWTH, STRUCTURE (2495)
 MORRIS, PROLIFERATION KINETICS (2050)
 MORRIS, TOTAL PROTEIN SYNTHESIS,
 ALBUMIN SYNTHESIS (0305)
 MORRIS, TRANSFER RNA, ALTERATIONS
 (2090)
 NOVIKOFF, NUCLEIC ACID SYNTHESIS, RAT
 (2544)
 NUCLEOSIDES, NUCLEOTIDES, GROWTH,
 RAT (2497)
 NUCLEOTIDE POOLS, NUCLEOSIDES (2497)
 ORNITHINE DECARBOXYLASE ACTIVITY
 (0315)
 PLASMA MEMBRANE OF LIVER CELLS,
 ATPASE ACTIVITY (0258)
 PREDNISOLONE, RNA SYNTHESIS, DNA
 SYNTHESIS, PHYTOHEMAGGLUTININ
 (0696)
 PULMONARY TUMORS, CYCLAMATE, MOUSE,
 REVIEW (0378)*
 REUBER H-35, FERRITIN, RAT (2550)
 REUBER MOUSE, ENZYMES (2549)
 RNA, RAT (2546)
 TRNA, PHENYLALANINE, MOUSE (2585)*
 TYROSINE TRANSAMINASE, CYCLOHEXIMIDE,
 PUROMYCIN (2551)
 HERBICIDE
 MONURON, CARCINOGENICITY, RAT, MOUSE
 (0897)
 HETEROGENIZATION
 SKIN, GRAFT, TUMOR (0057)
 HETEROKARYOCYTE
 ADENOVIRUS 12, PERMISSIVE AND NON-
 PERMISSIVE CELL FUSION (0611)
 HEXOSE
 PROTEIN-BOUND NEUTRAL, RADIATION,
 HEPATOCTIC ULTRASTRUCTURAL CHANGES
 (0546)
 HISTAMINE
 WHOLE BODY IRRADIATION, SKIN LESIONS,
 RAT (0139)*
 HISTOCHEMISTRY
 ADRENALS, WHOLE BODY IRRADIATION, RAT
 (1407)*
 MUCOSUBSTANCE, CERVICAL CARCINOMA
 (2109)
 HISTOGENESIS
 AMYLOID STROMA, THYROID, MEDULLARY

CARCINOMA, ELECTRON MICROSCOPY
 (2111)
 CANCER, EPIDEMIOLOGY, GEOGRAPHIC
 DIFFERENCES (0858)
 EMBRYONAL ADENOCARCINOMA, TESTIS,
 CHILDREN (0746)
 HAIR FOLLICLE, BASAL CELL EPITHELIOM,
 (0862)*
 MIXED TUMOR, SALIVARY GLAND, HUMAN
 (0251)
 TRANSPLANT, MAMMARY GLAND, ISOGRAFT
 (1665)
 HISTOLOGY
 RECTAL MUCOSA, EARLY CARCINOMA (1599)
 HISTOPATHOLOGY
 HODGKIN'S DISEASE, PATHOGENESIS, MAN
 (0748)*
 TUMOR, CELLULAR POLYMORPHISM,
 PARA-ADENOVIRUS TYPE 7, HAMSTER
 (2326)
 TUMOR, CHICK-EMBRYO-LETHAL-ORPHAN
 ADENOVIRUS (1459)
 HODGKIN'S DISEASE
 AGE, HISTOLOGY (0260)
 AGE DISTRIBUTION (1218)
 ANTIBODY TITERS, EPSTEIN-BARR VIRUS
 (1025)
 CANCER OF THE BLADDER, CHLORNAPHAZINE
 (0110)
 CHILDREN, INCIDENCE AND PATHOLOGY
 (0756)
 CONCURRENT LIVER CARCINOMA (1718)*
 EPSTEIN-BARR VIRUS, HERPES SIMPLEX,
 CYTOMEGALOVIRUS, ANTIBODY (0155)
 EPSTEIN-BARR VIRUS, VIRAL ANTIBODY
 TITERS (1434)
 GERMANY, EPIDEMIOLOGY (0272)
 HISTOLOGICAL EVOLUTION (1148)
 HISTOPATHOLOGY, PATHOGENESIS, MAN
 (0748)*
 HL-A ANTIGEN SPECIFICITY (0717)
 INCIDENCE, ENGLISH CHILDREN, AFRICAN
 CHILDREN (1607)
 JAPAN, EPIDEMIOLOGY (0271)
 LEUCOCYTE ANTIGENS (0718)
 LEUKEMIA, CANDIDA ALBICANS, RESISTANCE
 (2461)
 LYMPHOCYTES, PHYTOHEMAGGLUTININ CON-
 SUMPTION (0733)
 LYMPHOCYTES, PROLIFERATION KINETICS,
 PHYTOHEMAGGLUTININ (1720)*
 LYMPHOMA, THYMOMA, CONNECTIVE TISSUE
 ULTRASTRUCTURE (2113)
 LYMPHOSARCOMA, WALDENSTROM'S MACRO-
 GLOBULINEMIA, PLASMOCYTOMA,
 RETICULOSARCOMA, IMMUNOGLOBULINS
 (0734)
 PARANEOPLASTIC SYNDROME, IMMUNO-
 SUPPRESSION (2466)*
 SERUM ALKALINE PHOSPHATASE, ISOZYMES,
 HODGKIN'S LYMPH NODE (0246)
 SKIN INVOLVEMENT, SPREAD, MECHANISM
 (0821)
 SPONTANEOUS, CHEMICALLY INDUCED,
 ANIMALS, MAN, PATHOGENESIS, REVIEW
 (0019)*
 TONSILLECTOMY (2019)
 UGANDA, EPIDEMIOLOGY (2493)

RMONE

ACTH SYNDROME, OAT CELL CARCINOMA (2103)
ADRENAL GLAND, CARCINOMA, ADENYL CYCLASE (2537)
ANDROGEN SECRETION, ENDOCRINE
IMBALANCE, MAMMARY CARCINOMA (1751)*
ANDROGEN TREATMENT, PRAOMYS (MASTOMYS) NATALENSIS, PROSTATIC HYPERPLASIA (0885)
ANTIGENICITY, CARCINOMA (1740)
ANTITUMOR EFFECT, 7,12-DIMETHYLBENZ-(A)ANTHRACENE, MAMMARY GLAND, RAT (0457)
2-BR-ALPHA-CRYPTINE, GROWTH, MAMMARY CARCINOMA (0930)
CANCER ETIOLOGY, MAN, REVIEW (0385)*
CHANGES, CANCER PATIENTS, DISCRIMINANT FUNCTION (0372)
CHORIONIC GONADOTROPIN, RADIATION, ANDREOBLASTOMA (1594)
CHRONIC ESTROGENIC STIMULATION, EPIDERMIZATION OF ENDOMETRIUM, MONKEY CERVIX (1158)
CONTRACEPTIVES, CERVIX, UTERUS, EPITHELIAL ATYPIAS, HUMAN (0514)*
CONTRACEPTIVES, ENDOMETRIUM, REVIEW (0871)*
DEPENDENT, MURINE MAMMARY TUMORS (2112)
ECTOPIC PRODUCTION, HUMAN CHORIONIC SOMATOMAMMOTROPIN, NONTROPHOBLASTIC CANCERS (1656)
ESTRADIOL-17 BETA, LYMPHOID CELL PROLIFERATION, IN VITRO, LYMPHOSARCOMA, ACUTE LYMPHOBLASTIC LEUKEMIA, MAN (0342)*
ESTROGEN, BINDING, TUMOR RESPONSIVENESS (0834)
ESTROGEN, ENDOMETRIAL CARCINOMA, FALLOPIAN TUBES, EPITHELIAL HYPERPLASIA (1160)
ESTROGEN, ENZYME ACTIVITY, MAMMARY EPITHELIAL CELLS, RAT (2470)
ESTROGEN, POLYETHYLENE STRIPS, UTERINE TUBES, GUINEA PIG (0815)
ESTROUS CYCLE, DIMETHYLBENZANTHRACENE, MAMMARY GLAND CARCINOMA, RAT (1794)
GLUCOCORTICOID, INSULIN, GLUCOSE-6-PHOSPHATASE, DIETHYLNITROSAMINE (1814)
GONADOTROPHIN SECRETION, TROPHOBLASTIC DIFFERENTIATION, BRONCHIAL CARCINOMA (0774)
HYPERESTRINISM, PROGESTATIONAL DEFICIENCY, ENDOMETRIAL HYPERPLASIA, CERVICAL POLYPS (0742)
HYPOESTROGENISM, ENDOMETRIAL CANCER, CYTOLOGIC STUDY (1225)
HYPOTHALAMIC LESION, PROLACTIN, RAT MAMMARY TUMOR (0770)
HYPOTHYROIDISM, HYPERESTRINISM, 6-METHYLTHIOURACIL, MAMMARY GLAND CANCER, RAT (0886)
LOBULOALVEOLAR DIFFERENTIATION, MOUSE STRAIN DIFFERENCES (0769)
METHYLTHIOURACIL, L-THYROXINE, CASTRATION, DMBA, CERVICO-VAGINAL TUMORS IN RATS (0887)

OVARY, PULMONARY TUMORS, HYDRAZINE SULFATE (0910)
PLASMA GROWTH, HYPERTROPHIC OSTEOARTHROPATHY, CARCINOMA OF THE BRONCHUS (0773)
POSTCASTRATIONAL ADRENAL TUMORS, STRAIN VARIABILITY, MICE (1199)
PREGNANCY, 5-HYDROXYTRYPTAMINE, MAMMARY TUMOR DEVELOPMENT (1226)
PROGESTERONE, ESTROGEN, DNA AND RNA IN RAT PROSTATE (0889)
PROLACTIN, 7,12-DIMETHYLBENZANTHRACENE REGRESSION, RAT (2226)
PROLACTIN, MAMMARY CARCINOGENESIS INHIBITION (0440)
RAT LIVER, POLYRIBOSOMES, X-IRRADIATION (0544)
RESPONSIVENESS, 7,12-DIMETHYLBENZ(A)ANTHRACENE, MAMMARY TUMORS (0060)
SOMATOTROPIN, GLUCOSE EFFECT, MAMMARY GLAND CANCER, UTERINE CANCER, HUMANS (2469)
STEROID EQUILIBRIUM, BRAIN TUMORS, ETIOLOGY, REVIEW (0844)
STIMULATION OF TUMORIGENESIS, MAMMARY TUMOR (1215)
SYNESTROL, 7,12-DIMETHYLBENZ(A)ANTHRACENE, OSTEOSARCOMA, RABBIT (1329)
SYNESTROL, KIDNEY TUMORS, MORPHOGENESIS, HAMSTER (1586)
SYNTHESIS, TROPHOBLASTIC TUMOR CELLS, HUMAN CHORIOCARCINOMA (1653)
TESTOSTERONE, SYNESTROL, 7,12-DIMETHYLBENZ(A)ANTHRACENE, MAMMARY GLAND TUMOR, MOUSE (1145)
THYROCALCITONIN, MEDULLARY CARCINOMA, THYROID, URINE (1638)
TUMOR GROWTH, OVARIECTOMIZED RATS, YOSHIDA ASCITES SARCOMA (1214)
TUMOR REGRESSION, OVARIECTOMY, 7,12-DIMETHYLBENZ(A)ANTHRACENE (1327)
HUMAN CHORIONIC SOMATOMAMMOTROPIN NONTROPHOBLASTIC CANCERS, ECTOPIC PRODUCTION OF HORMONE (1656)
HYBRIDIZATION
CARCINOGENICITY, HAMSTER (1715)*
CHROMOSOME, EHRLICH'S TUMOR, TUMORIGENICITY (2514)
MALIGNANCY, CHROMOSOME (2554)
MICE, CARCINOGENESIS, KARYOLOGIC CHARACTERISTICS, HEREDITY (0838)
MURINE SARCOMA -180, L-5178Y LYMPHOBLAST, CHROMOSOME (1661)
POLYOMA, MOUSE, HAMSTER (2382)
SARCOMA, FIBROBLASTS, CHROMOSOMES, MURINE (2386)
SV40, ADENOVIRUS 2, DNA (2332)
HYDRAZINE
LUNG, LIVER, CARCINOMA, MOUSE, ISONIAZIDE METABOLISM, MAN (0415)
LUNG CANCER, GONADECOTOMY, MOUSE (0414)
SULFATE, OVARIAN HORMONE PRODUCTION, PULMONARY TUMORS (0910)
TOXICITY IN PREGNANT RATS (0043)
HYDROCARBON
CARCINOGENIC, NITROSAMINES, SPINACH (0880)*

POLYCYCLIC, CARCINOGENS, BRONCHIAL
CARCINOMA (0461)
POLYCYCLIC, PLANTS, AIR POLLUTANTS,
FOOD (0397)
HYDROCORTISONE
CHALONE, DNA SYNTHESIS, MOUSE
EPIDERMIS (2059)
DNA SYNTHESIS, LIVER, RAT (2262)
N-HYDROXY-2-ACETAMIDOFUORENE
EXCRETION, ADRENALECTOMY, BILE DUCT
LIGATION (0908)
N-HYDROXY-N-ACETYL-4-AMINOBIPHENYL
LIVER, NUCLEIC ACIDS, RAT (2181)
N-HYDROXY-ACETYLAMINOFUORENE
BINDING TO POLYRIBONUCLEOTIDES IN
VITRO (0406)
N-HYDROXY-2-ACETYLAMINOFUORENE
BINDING TO DNA, REPLICATION (1298)
4-HYDROXYAMINOQUINOLINE
MONOACETYL, SARCOMA INDUCTION IN MICE
(1359)
4-HYDROXYAMINOQUINOLINE-1-OXIDE
DERIVATIVES OF CARCINOGEN,
CARCINOGENICITY IN MICE AND RATS
(1827)
METABOLISM, LIVER, BLOOD, MICE (1358)
3-HYDROXYANTHRANILIC ACID
EARLY BENZIDINE CARCINOGENESIS, SERUM,
RAT (0911)
N-HYDROXY-N-2-FLUORENYLACETAMIDE
CARCINOMA, LIVER, RAT (0409)
PROTEIN ADDUCT, LIVER, RAT (0407)
N-HYDROXY-3-FLUORENYLACETAMIDE
FLUORENYLACETAMIDE, TRNA, BINDING,
RAT LIVER (1773)
N-HYDROXY-2-FLUORENYLBENZENE-SULFONAMIDE
ACTIVATION, RAT TISSUE (2183)
8-HYDROXYQUINOLINE
CARCINOGENICITY, MOUSE, RAT (0487)
7-HYDROXYTHEOPHYLLINE
MICE, AMYLOIDOSIS, RETICULOSARCOMA,
LUNG ADENOMA (1764)
5-HYDROXYTRYPTAMINE
MAMMARY TUMOR DEVELOPMENT (1226)
3-HYDROXYXANTHINE
IMMUNOSUPPRESSION, CORTISONE, RAT
(2188)
HYPERPLASIA
ALVEOLAR NODULES, MAMMARY GLAND,
PHENYLALANINE, MOUSE (2191)
ENDOMETRIAL, HYPERESTRINISM, CERVICAL
POLYPS (0742)
ENDOMETRIAL CARCINOMA (1282)
FAMILIAL ADENOMATOSIS, ENDOCRINE,
WERNER'S DISEASE, SURGERY, REVIEW
(1279)
FOCAL AVILLOUS, MOUSE DUODENUM,
DIETETIC PANTHENIC ACID DEFICIENCY
(0311)
INFLAMMATORY PAPILLARY, ORAL MUCOSA,
DENTURE IRRITATION (0737)
KUPFFER CELL, BILE DUCT EPITHELIUM,
AFLATOXIN B1, HAMSTER (0517)*
LIPID, RAT ADRENAL CORTEX, ANILINE
(0925)
RESERVE CELL, INCOMPLETE SQUAMOUS
METAPLASIA, CERVICAL NEOPLASTIC
CHANGE (1585)

HYPOXIA
POLYCYTHEMIA, TRANSFUSION, ERYTHRO-
POIETIN (0307)
IATROGENIC TUMOR
ANTICONVULSANT CHEMOTHERAPY,
OVARIAN THECOMA (1371)
CYTOSTATICS, IMMUNOSUPPRESSIVES, RAT
(0904)
MULTIPLE MYELOMA, ACUTE MYELOMONOCY-
LEUKEMIA, MELPHALAN (0507)
THYROTOXICOSIS, RADIOACTIVE IODINE
TREATMENT (0549)
2-IMIDAZOLIDINONE
NITRITE, WILMS' TUMOR, RAT (2184)
IMMUNITY
ACTIVE, CONGENITAL TUMOR, ADOPTIVE
IMMUNITY, MOUSE (1547)
ADENOVIRUS SA7, HAMSTER (0616)
ALLOGRAFT, ANTILYMPHOCYTE SERUM,
LYMPHOID CELLS, MICE (1559)
ALLOGRAFT SURVIVAL, X-IRRADIATION,
MOUSE LEUKEMIA CELLS (0225)
ANTIGENS, POLYOMA VIRUS, RAT (2454)
ANTIGENS, RHABDOMYOSARCOMA, MOUSE
(1987)
ANTI-LYMPHOCYTE SERUM, ROUS SARCOMA
VIRUS, QUAIL (2446)
ANTISARCOMA ANTIBODY, SKELETAL SARCO-
(0710)
ANTITUMOR REACTIONS, TUMOR ANTIGENS
(1754)*
ASCITES, PERITONEAL FLUID, PASSIVE
TRANSFER (1555)
AUTOCHTHONOUS TUMOR CELLS, LYMPHOCY-
RESPONSE, HUMAN (1574)
AUTOIMMUNE RESPONSE, LYMPHOID
NEOPLASIA, REVIEW (0009)
AVIAN LEUKOSIS, VIRAL ANTIGEN, CHIC
(1964)
CANCER, DEOXYCHOLATE, HUMANS, ANIMA-
(2465)*
CANCER, EXPERIMENTAL MODELS, MICE
(2405)
CANCER, VIRUS, RATS, MICE, REVIEW
(1734)
CARCINOMA, SARCOMA, LYMPHOCYTES,
HUMAN (2418)
CARCINOMA TRANSPLANT, LYMPHOCYTE
REACTION (2433)
CELLULAR AND HUMORAL IMMUNE RESPON-
GROSS VIRUS LYMPHOMA (1531)
COMPETENCE, LYMPHOID CELLS,
X-IRRADIATION (1544)
DEFECTIVE IMMUNE RESPONSE, SPLEEN,
RIDGEWAY SARCOMA IN MICE (1548)
EHRlich ASCITES TUMOR, SPLEEN CELLS
MICE (1999)
FIBROSARCOMA, METASTASIS, MICE (242)
FRIEND DISEASE VIRUS, MYCOBACTERIUM
BOVIS (1903)
FRIEND LEUKEMIA VIRUS, MACROPHAGE
MIGRATION (1534)
HUMAN CANCER, TUMOR SPECIFIC ANTIGE-
(0840)
HUMAN TUMORS, INHIBITORY FACTOR,
LEUCOCYTE MIGRATION (1545)
IMMUNE DEFICIENCY, PREDISPOSITION,
LYMPHOID MALIGNANCIES (1723)

IMMUNIZATION, LEUKEMIA, RADIATION
VIRUS (1968)
IMMUNOGENICITY, MAMMARY TUMOR VIRUS,
MICE (2402)
IMMUNOLOGICAL ABNORMALITIES, SIBLING
GROUP, LYMPHORETICULAR MALIGNANCIES
(1123)
INHIBITION OF MIGRATION, TUMOR
ANTIGENS, MACROPHAGE (1554)
ISOGRAFTS, SARCOMA, RNA MURINE (1988)
LYMPHOCYTES, MIGRATION INHIBITING
FACTOR, HEPATOMA, GUINEA PIG (2440)
LYMPHOCYTES, NEPHROBLASTOMA, HUMAN
(2015)
LYMPHOCYTES, PHYTOHEMAGGLUTININ (1137)
MELANOMA, TUMOR-SPECIFIC, HUMAN (2438)
MOLONEY VIRUS, RAUSCHER VIRUS, MOUSE
(0635)
PARASITE, TUMOR GROWTH, NEMATODE
INFECTION (2118)
PATHOLOGY OF VIRAL INFECTIONS, MURINE
SARCOMA VIRUS (1472)
POLYOMA, ROUS TUMOR, RATS (2455)
POLYOMA TRANSFORMED BHK, HYBRIDS,
SUPERINFECTION (2388)
RADIATION, MAMMARY CARCINOMA, MICE
(2416)
RNA-TRANSFERRED, 3-METHYLCHOLANTHRENE,
LIPOSARCOMA (0077)
SARCOMA, CELL-SURFACE ANTIGEN, HUMAN
(2016)
SARCOMA, RNA, BENZOPYRENE, RAT (2428)
SARCOMA TRANSPLANTATION, YEAST, MOUSE
(0705)
SEROLOGIC SPECIFICITY, FREUND ADJUVANT
TRNA, METHYLATION (2089)
SERUM IMMUNOGLOBULINS, CHRONIC LYMPHO-
CYTIC LEUKEMIA (2011)
SIMIAN ADENOVIRUS POPULATION,
HUMAN ADENOVIRUS POPULATION (1457)
SKIN GRAFTS, LYMPHOSARCOMA, MICE
(1558)
SULFANILIC ACID-CONJUGATED ANTIGENS,
OVARIAN ASCITES TUMOR, RAT (0732)
SURVEILLANCE, 3-METHYLCHOLANTHRENE,
MICE (2424)
TRANSFER, IMPAIRMENT, GUINEA PIG
HEPATOMA (1992)
TRANSFER, RNA FROM TUMOR-IMMUNE
ANIMALS, BENZ(A)PYRENE (0728)
TRANSPLANT, LYMPHOID CELL REACTION
(2408)
TRANSPLANTATION, TUMOR CELL EXTRACTS,
ADENOVIRUS 12 (1055)
TUMOR, HAMSTER, SV40 (1979)
TUMOR, LEUKEMIA (2159)
TUMOR, LYMPH NODE (2462)
TUMOR, RNA, GUINEA PIG (2464)*
TUMOR, SPLEEN CELL, MOUSE (2459)
TUMOR HETEROGRAFT, DIET, RAT (2401)
TUMOR SURVIVAL TIME, YEAST RNA, MICE
(1556)
TUMOR TRANSPLANT, 7,12-DIMETHYLBENZ-
(A)ANTHRACENE, SIMIAN ADENOVIRUS 7
(1982)
TUMOR TRANSPLANTATION, 6-METHYL-
CHOLANTHRENE, INHIBITION OF IMMUNE
RESPONSE (1551)

X-IRRADIATION, LYMPHOMA CELLS, MOUSE
(2289)
IMMUNIZATION
CYTOLYTIC POTENCY, MOUSE LEUKEMIA
ANTISERA, RABBIT (1553)
ROUS SARCOMA VIRUS, CHICKEN (2436)
IMMUNOCYTOMA
IMMUNOGLOBULIN, REVIEW (1737)
IMMUNOFLUORESCENCE
MICROSCOPY, BONE MARROW, ACUTE
LEUKOSIS, ACUTE MYELOSIS, CHILDREN
(0233)
IMMUNOGLOBULIN
A, HAPTEN, MYELOMA (2008)
A, MYELOMA, HUMAN (2007)
ALPHA2-GLOBULIN, RADIATION, BLOOD,
BONE MARROW (2278)
ALPHA2-GLOBULIN, RADIATION, BONE
MARROW, MOUSE (2276)
ANTIGEN-BINDING, MYELOMA PROTEINS,
M-COMPONENTS (1736)
BIOSYNTHESIS, PLASMA CELL, MYELOMA
(0720)
CARBOHYDRATE, BIOSYNTHESIS, MOUSE
PLASMA CELL TUMOR (1565)
CARCINOMA, MELANOMA, SARCOMA, HUMAN
(2419)
DEFICIENCY, MACROGLOBULINAEMIA,
MYELOMATOSIS, HUMAN (2451)
IGG, MYELOMA, LIGHT AND HEAVY POLY-
PEPTIDE CHAINS (0226)
IGG2, BENZO(A)PYRENE-INDUCED MOUSE
TUMORS (1133)
IGG3, MOUSE SERUM, MURINE MYELOMA (1568)
IGM DYSPROTEINEMIA, ACUTE MYELOMA
(1128)
IMMUNOCYTOMA, REVIEW (1737)
ISOANTIGENS, BURKITT'S LYMPHOMA, HUMAN
(2158)
LIVER, CARCINOMA, CIRRHOSIS (0232)
LYMPHOMA, GOLGI COMPLEX, ENDOPLASMIC
RETICULUM (2009)
LYMPHOMA, MICE (2441)
LYMPHOSARCOMA, WALDENSTROEM'S
MACROGLOBULINEMIA, PLASMOCYTOMA,
HODGKIN'S DISEASE (0734)
MURINE PLASMOCYTOMA, CELL CULTURE OF
TUMOR (1546)
MYELOMA, IGG2B, MOUSE (2005)
MYELOMA, LIPIDS, MAN (2445)
MYELOMA, PROTEIN, HUMAN (2443)
PLASMA CELL TUMORS, TRNA, ISOACCEPTING
RETICULOCYTES, MICE (2504)
SPLEEN AND LYMPH NODE IGM, BOVINE
LEUKOSIS (2013)
SYNTHESIS, RNA, MYELOMA, MOUSE (2450)
TUMOR, IGG, IGA (0229)
URINE, CANCER PATIENTS, LIGHT CHAIN
(1139)
URINE AND SERA, BURKITT'S LYMPHOMA
(0573)
IMMUNOLOGY
ADENOVIRUS TYPE 8, TYPE 9, CROSS
REACTIVITY (1054)
ADENOVIRUS TYPE 12, TUMOR, MOUSE
(1456)
ANTIBODY TO FLAGELLIN, CANCER
PATIENTS, SURVIVAL TIME (1119)

ANTIGENIC VARIABILITY, POLYOMA VIRUS, MOUSE (2391)
 ANTIGENICITY, SPONTANEOUSLY TRANSFORMING MOUSE CELLS (1120)
 ANTITHYMOCYTE SERUM, SPLENIC LYMPHOID TUMORS, POLYOMA VIRUS (0682)
 ANTITUMOR ANTIBODIES, SARCOMAS IN MICE METHYLCHOLANTHRENE (0943)
 BURKITT'S LYMPHOMA, NASOPHARYNGEAL, CARCINOMA (0151)
 CANCER, RESISTANCE TO TUMOR (1142)*
 CARCINOMA, OVARY, UTERUS, MAMMARY GLAND (1135)
 CARRIER AGENTS, TUMOR VACCINES, ANTIGENIC 'OTHERNESS' (0356)
 CHEMICALLY-INDUCED TUMORS, VIRAL TUMORS, REVIEW (0361)
 CONTACT SENSITIVITY, 7,12-DIMETHYLBENZ(A)ANTHRACENE, GUINEA PIGS (1324)
 CROSS IMMUNIZATION, VIRUS, MURINE LEUKEMIA VIRUS, INTERFEROGENESIS (0595)
 CROSS-REACTION, AVIAN LEUKOSIS GROUP-SPECIFIC ANTIGEN, HUMAN LEUKEMIC PLASMA (1126)
 7,12-DIMETHYLBENZ(A)ANTHRACENE, GAMMA-2-GLOBULIN, FREUND ADJUVANT, METASTASES, RAT (0455)
 EMBRYO SPECIFIC ANTIGEN, CANCER TISSUE MOUSE (0721)
 ENHANCEMENT OF TUMOR ISOGRAFT, RNA FROM TUMOR-IMMUNIZED ANIMALS (1561)
 ESTROGEN DEPENDENT MAMMARY TUMOR, IMMUNIZATION, GROWTH (1993)
 FERRIDEXTRAN SPOFA-INDUCED SARCOMA, TRANSPLANTABILITY, KARYOTYPE (0706)
 GAMMA-2-GLOBULIN, URINE, IMMUNOELECTROPHORESIS (0731)
 GENITAL HERPES SIMPLEX VIRUS, ANTIBODIES, HUMAN CERVIX CARCINOMA (0186)
 HAMSTER-SPECIFIC C-TYPE VIRUS, GROUP SPECIFIC VIRION ANTIGEN (0552)
 HEMADSORPTION REACTION, LEUKEMIA, FELINE, HUMAN (1976)
 HOST RESPONSE TO TUMOR TRANSPLANT, REGIONAL LYMPH NODES (1125)
 IMMUNE DEFICIENCIES, TUMORIGENESIS, LYMPHOMAS (0354)
 IMMUNE LYMPHOID CELL, MURINE LYMPHOMA, MACROPHAGE (0725)
 IMMUNE RESPONSE, LYMPHOCYTE PROLIFERATION, LYMPHOPROLIFERATIVE DISEASE, REVIEW (0391)*
 IMMUNE RESPONSE, MINERAL OIL TUMORIGENESIS, SUSCEPTIBILITY (0894)
 IMMUNIZATION, TUMORIGENESIS INHIBITION SV40 (0671)
 IMMUNO-ACCELERATOR, LENTINAN (1583)*
 IMMUNOCOMPETENCE, IMMUNOTHERAPY, HUMAN MELANOMAS AND SARCOMAS (0704)
 IMMUNOCYTE CLONAL EVOLUTION, AUTO-IMMUNE DISEASE, LYMPHOSARCOMA (0719)
 IMMUNOHEMOLYTIC ANEMIA, YOSHIDA SARCOMA CELLS, PENETRATION OF ANTITUMOR ANTIBODIES (0709)
 IMMUNOLOGICAL SURVEILLANCE (0355)
 IMMUNOPATHOLOGICAL PROFILE, TUMOR PROFILE, MOUSE STRAINS (0393)*
 IMMUNOSUPPRESSIVE DRUGS, RENAL TRANSPLANTATION, CERVICAL DYSPLASIA (0693)
 IMMUNOSUPPRESSIVE THERAPY, MAMMARY ADENOCARCINOMA (0695)
 LEUKEMIA, CELLS, HUMAN (2406)
 LYMPHOCYTES, EPSTEIN BARR VIRUS, ANTIGEN, DELAYED HYPERSENSITIVITY, HUMAN (2421)
 LYMPHOEPITHELIAL TYMOMA, ORGAN TRANSPLANT, MAN (0360)
 LYMPHOMA, INACTIVATION, RADIATION, MOUSE (0223)
 MAMMARY GLAND, CARCINOMA, RAT, 7,12-DIMETHYLBENZ(A)ANTHRACENE (0454)
 MAMMARY GLAND TUMOR, LEUKEMIA, MOUSE (2410)
 MAREK'S DISEASE, HERPESVIRUS, VIRUS (1468)
 MELANOMA, LYMPHOCYTE STIMULATION, TUMOR EXTRACT (0230)
 MOUSE EMBRYO FIBROBLAST CULTURE, VIRAL ETIOLOGY FOR 'SPONTANEOUS' TRANSFORMATION (1072)
 MYELOMA, GAMMA A PROTEIN (0715)
 MYELOMA PROTEINS, MEDULLARY AND EXTRAMEDULLARY PLASMACYTOMA (2020)*
 NEOPLASM, MACROPHAGE MIGRATION, DELAYED HYPERSENSITIVITY REACTION (0228)
 POLYOMA VIRUS, TRANSFORMED MOUSE CELLS, IMMUNE SERUM TREATMENT (1104)
 PREGNANT MOTHERS, OFFSPRING IMMUNITY, LEUKEMIA, GROSS VIRUS (1449)
 RETICULOENDOTHELIAL SYSTEM, VIRUS (0882)*
 RHABDOMYOSARCOMA, CYTOTOXIC FACTOR, MOUSE (2432)
 ROUS SARCOMA VIRUS, ANTIGEN COMPLEX, CHICK CELLS (1527)
 SEROLOGICAL STUDY, CHILDHOOD NEOPLASM (2021)*
 SEROLOGY, RNA TUMOR VIRUS, HAMSTER (2395)*
 SERUM ANTIBODIES, INFECTIOUS MONONUCLEOSIS, EPSTEIN-BARR VIRUS (0577)
 SERUM FRACTIONS, RAUSCHER VIRUS, MOUSE (1448)
 SV40, SENSITIVITY, HAMSTER (2449)
 THYMUS, LYMPHOCYTES, IRRADIATION, MICE (0842)
 THYMUS, NEOPLASIA, REVIEW (1272)
 TONSILLECTOMY, HODGKIN'S DISEASE (2019)
 TUMOR, FRIEND VIRUS, RAT (2411)
 TUMOR, HOST RESPONSE, COLONY FORMING CELLS, MICE (2404)
 TUMOR CELL INOCULA, RETARDATION OF PRIMARY TUMOR GROWTH, BENZO(A)PYRENE (0940)
 TUMOR IMMUNE RESPONSE IN HUMANS, TUMOR ANTIGENICITY (0841)
 TUMOR INCIDENCE, PHENOTYPE, BLOOD GROUPS, REVIEW (1284)*

TUMOR-SPECIFIC, TRANSPLANTATION,
 ANTIGEN, GLYCOPROTEINS, REVIEW
 (1758)*
 TUMOR-SPECIFIC, TRANSPLANTATION,
 ANTIGEN, HUMAN, REVIEW (0358)
 UREA-EXTRACTABLE ANTIGENS, BENIGN AND
 MALIGNANT TUMORS, NORMAL MOUSE
 EPIDERMIS (0726)
 VIRAL INTERFERENCE, FELINE LEUKEMIA
 COMPLEX (2311)
 NODOPROLIFERATIVE DISEASE
 LYMPHOSARCOMA, PLASMOCYTOMA, HODGKIN'S
 DISEASE, IMMUNOGLOBULINS (0734)
 NOSUPPRESSION
 ADENOCARCINOMA, THYMECTOMY, RADIATION,
 MICE (1552)
 ALKYLATING AGENTS, RATS, MICE (0906)
 ANTIGENIC STIMULATION, LYMPHOMA
 DEVELOPMENT (1539)
 ANTILYMPHOCYTE SERUM, 3-METHYLCHOL-
 ANTHRENE, MICE (1540)
 ANTITHYMOCYTE SERUM, SQUAMOUS
 CARCINOMAS, DMBA (1325)
 AZATHIOPRINE, CHROMOSOMAL MUTATIONS,
 HUMAN LEUKOCYTES, METAPHASES (1766)
 BURKITT'S LYMPHOMA, VIRUS (0687)*
 CARCINOMA PATIENTS, SUPPRESSION OF
 IMMUNOCOMPETENCE, SURGERY (1116)
 CYTOSTATICS, CARCINOGENIC EFFECTS,
 RATS (0904)
 HAMSTER, ROUS SARCOMA VIRUS (2360)
 HODGKIN'S DISEASE, PARANEOPLASTIC
 SYNDROME (2466)*
 3-HYDROXYXANTHINE, CORTISONE, RAT
 (2188)
 IMURAN, STEROIDS, EARLY THYMECTOMY,
 ANTI-LYMPHOCYTE SERUM, ONCOGENICITY,
 REVIEW (0357)
 KIDNEY TRANSPLANT, CERVICAL CARCINOMA
 (1582)*
 LIVER, DIETHYLNITROSAMINE, RAT
 (1815)
 LYMPHOMA, ANTILYMPHOCYTE SERUM, MOUSE
 (2431)
 MAMMARY TUMOR VIRUS, ALLOGRAFT
 SURVIVAL (1530)
 MOUSE SPLEEN, FRIEND LEUKEMIA VIRUS
 (1529)
 MURINE LEUKEMIA TRANSPLANT, NORMAL
 TISSUE RNA (1557)
 ORGAN TRANSPLANT, LYMPHOMAGENESIS,
 ANTIGEN STIMULATION (1589)
 ORGAN TRANSPLANTATION, MALIGNANT
 TUMORS (0839)
 PAPOVA SV40 VIRUS, HUMAN ADENOVIRUS
 TYPE 16, SENDAI VIRUS, HAMSTER
 (1042)
 POLYOMA VIRUS, RESTORATION OF IMMUNO-
 COMPETENCE (1117)
 RADIATION, LANDSCHUTZ ASCITES,
 GROWTH, RAT (2496)
 THERAPY, ORGAN TRANSPLANT, DEVELOPMENT
 OF MALIGNANCY (1118)
 TRANSPLANTATION OF TUMORS, BOVINE
 LYMPHOSARCOMA (2012)
 TUMOR, POLYOMA VIRUS (1113)
 URETHAN, 7,12-DIMETHYLBENZ(A)ANTHRA-
 CENE, RAT (1989)

IMMUNOTHERAPY
 POLYOMA VIRUS INDUCED, U.V. IRRADIA-
 TION, EXTRACT, HAMSTER (0241)*
 INDOLE
 DIETARY, 2-ACETYLAMINOFLUORENE,
 URINARY BLADDER TUMORS (0907)
 INDUCTION
 INFECTIVITY, SV40, MITOMYCIN C, OTHER
 AGENTS (0660)
 INFECTIOUS MONONUCLEOSIS
 ACUTE LYMPHATIC LEUKEMIA, CONCURRENT
 COURSES OF DISEASE (1237)
 ACUTE LYMPHOCYTIC LEUKEMIA,
 EPSTEIN-BARR VIRUS (1578)
 BURKITT'S TUMOR, EPSTEIN-BARR VIRUS
 (0154)
 EPSTEIN-BARR VIRUS (0353)
 EPSTEIN-BARR VIRUS, ANTIBODIES (0577)
 INFECTIVITY
 DIFFERENTIAL, VIRAL SEROLOGICAL TYPE,
 HERPESVIRUS HOMINIS (1460)
 MURINE SARCOMA, VIRUS, TRANSFORMATION
 (1068)
 RAT VIRUSES, HEMAGGLUTINATION-INHIBI-
 TION (0559)
 RAUSCHER LEUKEMIA VIRUS, CELL
 PERMEATION, MOUSE (2318)
 SV40, DNA, SUPERHELICAL, NICKED (1951)
 VIRUS, HETEROGENEITY, AVIAN ERYTHRO-
 BLASTOSIS (1437)
 INFILTRATION
 EHRlich ASCITES TRANSPLANT, MYELIN
 BREAKDOWN, BRAIN, WHITE MOUSE
 (0253)
 MALIGNANT, CELLULAR BLUE NEVUS, BRAIN
 (1698)
 INFRARED EMISSION
 PAPILLOMA (0334)*
 INHIBITOR
 5-BROMODEOXYURIDINE, RAT HEPATOMA
 CELLS, TYROSINE AMINOTRANSFERASE
 (2078)
 DNA IODODEOXYPYRIDINE, CYTOSINE
 ARABINOSIDE, BURKITT'S LYMPHOMA
 (1971)
 FACTOR, LEUCOCYTE MIGRATION, HUMAN
 TUMORS (1545)
 HERPES VIRUS, GIANT CELL FORMATION,
 RABBIT KIDNEY, COMPOUND 48/80
 (0188)
 INTERFERON, POLY I:C, MAMMARY
 CARCINOMA, MOUSE (2346)
 LENTINAN, IMMUNO-ACCELERATOR (1583)*
 TRANSPORT, GROWTH URIDINE, PHOSPHATE,
 3T3 (1960)
 INSULIN
 MAMMARY CARCINOMA, DIMETHYLBENZ(A)
 ANTHRACENE, RAT (0450)
 INTERCALATION
 POLYADENYLIC ACID, POLYCYCLIC HYDRO-
 CARBONS (0410)
 INTERFERON
 CHICKEN LEUKOCYTES, HUMAN ADENOVIRUS
 TYPE 12 (1045)
 EMBRYO CELLS, POLYINOSINIC POLYCYTIDY-
 LIC ACID, VIRUS (0953)
 ENDOGENEOUS, DEFENSE AGAINST ONCOGENIC
 VIRUSES, REVIEW (0021)*

FIBROBLASTS, LEUKEMIA, SARCOMA, VIRUS (1528)
 INDUCTION, CHICK EMBRYO CELLS, ADENOVIRUS, VIRUS (0178)
 INDUCTION, HAMSTER, POLYOMA VIRUS (1519)
 INTERFEROGEN, MURINE LEUKEMIA VIRUS, CROSS IMMUNIZATION (0595)
 LEUKEMIA, LEUKOCYTES (0335)*
 LEUKEMIA, VIRUS, LACTATE DEHYDROGENASE (1454)
 MORTALITY, HARVEY MURINE SARCOMA VIRUS (0639)
 POLY I:C, HERPESVIRUS SAIMIRI (1918)
 POLY I:C, INHIBITOR, MAMMARY TUMOR, MOUSE (2346)
 TRANSFORMATION, POLYOMA, BHK (2390)
 3T3 CELL CULTURE, POLYOMA VIRUS, TEMPERATURE-SENSITIVE POLYOMA MUTANT DNA (0678)
 INTESTINE
 BACTERIA, CARCINOMA OF THE COLON, EASTERN AND WESTERN NATIONS (1189)
 CAPILLARIES, GAMMA RAY IRRADIATION, FRACTIONATED DOSE (1383)
 CARCINOMA, ADENOMATOUS POLYPS, SOUTH AFRICAN BANTU (0759)
 CARCINOMA, POLYP, CHROMOSOME (0325)
 CARCINOMA, SULFATED MUCOSUBSTANCES, COLONIC AND RECTAL (2066)
 CECUM, AMEBIC GRANULOMA, ADENOCARCINOMA (2123)
 CHRONIC ULCERATIVE COLITIS, BILIARY TRACT CANCER (1708)*
 COLON AND RECTUM, JUVENILE POLYP (1591)
 COLONIC MUCOSA, CARCINOMA, 35 SULFUR UPTAKE (2069)
 COLORECTAL CARCINOMA, FATHER AND SON OCCURRENCE (1696)
 1,2-DIMETHYLHYDRAZINE, CARCINOMAS, PAPILLOMAS (0044)
 DISTAL SMALL BOWEL BYPASS, 7,12-DIMETHYLBENZ(A)ANTHRACENE, MAMMARY ADENOCARCINOMA (1792)
 HYPERPLASIA, HYPERTHYROIDISM, RAT (0740)
 METAPLASIA, EPIDEMIOLOGY, JAPAN (2489)
 RECTAL CANCER, GASTRIC SURGERY, ESOPHAGEAL CANCER (1228)
 ULCERATIVE COLITIS, BILE DUCT CARCINOMA (1249)
 INTRACISTERNAL VIRAL PARTICLES
 MURINE LEUKEMIC TISSUES, VIRUS (1442)
 INTRAUTERINE CONTRACEPTIVE DEVICE
 ENDOMETRIAL HYPERPLASIA (1706)
 HORMONAL, CANCER, ANIMALS (1742)
 IODINE
 PHAGOCYTOSIS, LEUKEMIA, HUMAN (2063)
 RADIOACTIVE, BOMB FALLOUT, THYROID NEOPLASIA (0529)
 THYROID, PARATHYROID, NEOPLASTIC HUMAN (1635)
 IODINE 131
 THYROID, PAPILLARY ADENOCARCINOMA (0126)
 IRAN
 EPIDEMIOLOGY, CERVIX, SKIN, BREAST (0284)

ISONICOTINIC ACID HYDRAZIDE
 TREATED WATER CONSUMPTION (0513)*
 ISOPROTERENOL
 CYTOPLASMIC RNA SYNTHESIS, CELL PROLIFERATION (0309)
 MOUSE KIDNEY CELLS, PROLIFERATION (1674)
 JAW
 AMELOBLASTOMA, DENTAL CYST (0244)
 GRANULAR CELL AMELOBLASTOMA, ULTRASTRUCTURE, HUMAN (2568)
 PAROSTEAL SARCOMA, OSTEOGENIC SARCOMA (0535)
 JEJUNUM
 MUCOSAL CRYPT CELLS, CELL SURVIVAL REPAIR, X-RAY AND NEUTRON IRRADIATION (0524)
 KARYOTYPE
 DIETHYLNITROSAMINE, LIVER, SPLEEN, RAT (2243)
 LYMPHOMA, LANDSCHUTZ (2524)
 RING CHROMOSOME, BENIGN HUMAN MENINGIOMA (2092)
 KERATOSIS
 SOLAR, SKIN CANCER, EXPOSURE TO SUNBURN (0269)
 KIDNEY
 CELLS, C-TYPE VIRUS PARTICLES, PICOGRAM (1428)
 CELLS, RNA SYNTHESIS INHIBITION, H-1 VIRUS, HUMAN (1099)
 DIMETHYLNITROSAMINE, HISTOLOGY OF TUMORS, RAT (1810)
 DNA, SV40, BSC-1 CELLS (1492)
 EPITHELIAL HYPERPLASIA, DIMETHYLNITROSAMINE, TRANSPLACENTAL EFFECT, MOUSE (0477)
 FENAL CARCINOMAS, FORMIC ACID 2-(4-NITRO-2-FURYL)-2-THIAZOLYL)HYDRAZIDE (0037)
 GIANT RENAL CYST, ADENOCARCINOMA, IRRADIATION (1861)*
 GLOMERULONEPHRITIS, GROSS LEUKEMIA VIRUS, ANTIBODIES, MOUSE (1034)
 HERPES TYPE VIRUS, TUMOR, FROG (2346)
 MESENCHYMAL TUMORS, RAT, DIMETHYLNITROSAMINE (0950)
 MOLONEY MURINE SARCOMA VIRUS, TRANSFORMATION IN VITRO (1937)
 MOUSE, GAS PHASE OF CIGARETTE SMOKE CYTOCHEMISTRY (0501)
 MOUSE, POLYOMA VIRUS, DNA SYNTHESIS, T-ANTIGEN (0676)
 NEPHROBLASTOMA, CHROMOSOMES, INFANT KARYOTYPE (1685)
 NEPHROBLASTOMA, DIETHYLSTILBESTROL, HAMSTER (1373)*
 NEPHROBLASTOMA, LYMPHOCYTES, IMMUNOLOGIC REACTION, HUMAN (2015)
 RENAL ADENOCARCINOMA, TUMOR-FREE POPULATION, LEOPARD FROG (0896)
 RENAL ADENOCARCINOMA, ULTRASTRUCTURE, DIMETHYLNITROSAMINE (1809)
 RENAL CARCINOMA, LYSOSOMAL ENZYME ACTIVITY, LIVER (1645)
 RENAL CARCINOMA, PROTEIN DEFICIENT RATS, DIMETHYLNITROSAMINE (0954)
 RENAL MESENCHYMAL TUMOR, DIMETHYLNITROSAMINE (0954)

NITROSAMINE, ULTRASTRUCTURE, RAT (1807)
 RENAL MESENCHYMAL TUMOR, PROGRESSION OF NEOPLASTIC CHANGES, DIMETHYLNITROSAMINE (1808)
 RENAL TUMORS, CLEAR CELL, RATS (1352)
 RENAL TUMORS, HEPATECTOMY, DIETHYLNITROSAMINE, RAT (1812)
 RIOPELLE'S TUMOR, HISTOGENESIS, REVIEW (0371)
 RNA POLYMERASE, AFLATOXIN B1, MOUSE (2207)
 RNA VIRUS, CHICKS, AVIARY MYELOBLASTOMA (1436)
 SV40 VIRUS, THYMIDINE KINASE, HAMSTER (0667)
 THOROTRAST, HUMANS (1404)*
 THOROTRAST, TUMORS (0366)
 TUMOR, DIET, DIMETHYLNITROSAMINE RATS (0952)
 TUMOR, MAMMARY GLAND TUMOR, MOUSE (0811)
 TUMOR, RENAL PELVIS, CORAL CALCULUS, PATHOGENESIS (1600)*
 ETICS
 CELL DEPLETION, INTESTINE, MOUSE (2282)
 CELL POPULATION, CAPILLARY ENDOTHELIAL CELLS, MOUSE MAMMARY TUMOR (0762)
 SIMIAN VIRUS 40, NEOPLASM, HUMAN, HAMSTER (0289)
 TUMOR SPECTRUM, URETHAN, AGE (0492)
 RIMAL GLAND
 TUMOR, MALIGNANT TRANSFORMATION (1149)
 TATION
 LACTOSE, 7,12-DIMETHYLBENZ(A)ANTHRACENE, MAMMARY GLAND, FIBROADENOMA, RAT (2223)
 PREGNANCY, BREAST CANCER (0321)
 YNX
 LARYNGITIS, CHRONIC, PAPILLOMA, PRE-CANCEROUS CHANGES (1152)
 NORMAL AND NEOPLASTIC TISSUES, CELL PROLIFERATION KINETICS, HUMAN (2051)
 OCCUPATIONAL EXPOSURE, 3,4-BENZOPYRENE (0117)*
 D
 CHROMOSOME DAMAGE, CYTOGENESIS (0112)
 UKEMIA
 ACUTE, CHRONIC MYELOGENOUS, CHRONIC LYMPHATIC, HAPTOGLOBIN (2010)
 ACUTE, KARYOTYPE STUDIES, LYMPHOBLASTOID CELLS IN VITRO (1693)
 ACUTE, MEDULAR APLASIA, CHLORAMPHENICOL, CASE REPORT (1375)*
 ACUTE, MELANOMA, ANTIGENICITY (1129)
 ACUTE, NON-PROLIFERATING CELLS, DNA, UV IRRADIATION (1223)
 ACUTE, OCCUPATIONAL EXPOSURE, CHLOROPHENOTHANE, BENZENE HEXACHLORIDE (0509)
 ACUTE, PROLIFERATIVE KINETICS, METHODS, REVIEW (0876)*
 ACUTE GRANULOCYTIC, CYTOGENETICS, HUMAN (2582)*
 ACUTE LYMPHATIC, INFECTIOUS MONONUCLEOSIS, CONCURRENT COURSES OF DISEASE (1237)

ACUTE LYMPHOCYTIC, EPIDEMIOLOGY, CHILDREN (1603)
 ACUTE LYMPHOCYTIC, EPSTEIN-BARR VIRUS, INFECTIOUS MONONUCLEOSIS (1578)
 ACUTE LYMPHOCYTIC, FAMILIAL AGGREGATION (0796)
 ACUTE LYMPHOCYTIC, MALIGNANT LYMPHOMA, HERPESVIRUS SAIMIRI (1464)
 ACUTE LYMPHOCYTIC, PHILADELPHIA CHROMOSOME (0130)
 ACUTE MONOMYELOGENOUS, AVIAN LEUKOSIS GROUP-SPECIFIC ANTIGEN, IMMUNOLOGIC CROSS-REACTION (1126)
 ACUTE MYELOBLASTIC, DI GUGLIELMO'S SYNDROME, PH1 CHROMOSOME CONDITION (1252)
 ACUTE MYELOGENOUS, CYTOSTATIC TREATMENT, METASTASIZING OVARIAN CARCINOMA (0506)
 ACUTE MYELOGENOUS, PH1 CHROMOSOME, ANEUPLOIDY (0798)
 ACUTE MYELOID, FRIEND VIRUS, EHRLICH ASCITES TUMOR, POLIOVIRUS, ECHOVIRUS RNA (0572)
 ACUTE MYELOID, RAPID BONE GROWTH, ADOLESCENCE (0375)
 ACUTE MYELOMONOCYTIC, ACUTE MYELOGENOUS, GRANULOCYTE KINETIC STUDY (0290)
 ACUTE MYELOMONOCYTIC, MELPHALAN THERAPY, MULTIPLE MYELOMA (0507)
 ADENOVIRUS, STRONTIUM 90, SWINE (1838)
 AGE DEPENDENT VARIATION, RH NEGATIVITY (0801)
 ANTIGEN, ASCITES (1549)
 ANTIGEN, ISOLATION, MAN (1141)*
 ANTIGEN, THYMUS-LYMPHOID TISSUE (1121)
 ANTISERA, IMMUNE REACTION IN RABBIT, CYTOLYTIC POTENCY (1553)
 ASCITIC, L-ASPARAGINASE, ANTIBODY (1560)
 AUTOCHTHONOUS LYMPHOCYTE STIMULATION (1995)
 AVIAN MYELOBLASTOSIS VIRUS, TRANSFORMED CELLS, RNA (1026)
 BACTERIA, TUMORS (2124)
 BLAST CELL, IGA PARAPROTEINEMIA, BENCE JONES PROTEIN (0713)
 BLOOD DYSCRASIA, IMMUNITY, MYCOPLASMA (0310)
 BONE MARROW, PROLIFERATION (2170)*
 BONE MARROW CELL, PERIPHERAL BLOOD CELL, HUMAN (0779)
 BURKITT'S LYMPHOMA, INFECTIOUS MONONUCLEOSIS, EPSTEIN-BARR VIRUS (0004)
 C-VIRUS, GS ANTIGEN, RODENT (2457)
 CARCINOMA, COMBINED CASES (2578)*
 CELL, IMMUNOLOGY, HUMAN (2406)
 CELL CYCLE, TUMOR GROWTH KINETICS, HUMAN (1281)
 CELL-FREE ORGAN EXTRACTS, MURINE MYELOID LEUKEMIA (0605)
 CHILDHOOD, EXPOSURE TO CATS (1604)
 CHILDREN, SPACE-TIME CLUSTERING, SAN FRANCISCO (0278)
 CHLOROLEUKEMIA, GRANULOCYTIC, KARYOTYPE STUDIES, RAT (1803)

CHROMOSOMAL ABNORMALITY, HUMAN,
HEMATOLOGICAL DISORDER (0800)
CHROMOSOMAL ABNORMALITY, REVIEW, HUMAN
(2175)*
CHROMOSOMAL ANOMALIES, DOWN'S
SYNDROME, BLOOM'S SYNDROME, REVIEW
(1756)*
CHROMOSOME, ABNORMALITY (2577)*
CHROMOSOME, BENZENE, PANCYTOPENIA
(2273)*
CHRONIC LYMPHATIC, ABNORMAL PHOSPHO-
GLUCOMUTASE ISOZYME (0794)
CHRONIC LYMPHOCYTIC, A1/G CHROMOSOME,
GAMMAGLOBULIN (0234)
CHRONIC LYMPHOCYTIC, LYMPHOID CELL,
ELECTROPHORETIC PATTERNS (1212)
CHRONIC LYMPHOCYTIC, PHYTO-
HEMAGGLUTININ, RNA METHYLASE
ACTIVITY (2091)
CHRONIC LYMPHOCYTIC, PLASMA, DNA
POLYMERASE (2082)
CHRONIC LYMPHOCYTIC, RNA, HUMAN (2517)
CHRONIC LYMPHOCYTIC, SERUM IMMUNO-
GLOBULINS (2011)
CHRONIC LYMPHOCYTIC, SKIN CANCER,
ETIOLOGY (0318)
CHRONIC MYELOCYTIC, PHILADELPHIA
CHROMOSOME (1730)
CHRONIC MYELOCYTIC, PH1 CHROMOSOME-
NEGATIVE MARROW CELLS (1235)
CHRONIC MYELOGENOUS, ATYPICAL KARYO-
TYPE, MISSING G GROUP CHROMOSOME
(1690)
CHRONIC MYELOGENOUS, STORAGE CELL
ULTRASTRUCTURE, GAUCHER'S DISEASE
(2110)
CHRONIC MYELOID, CYTOGENETICS AND
CARCINOGENESIS, PHILADELPHIA
CHROMOSOME (0344)
CHRONIC MYELOID, PLATELETS, ADENOSINE
DEAMINASE ACTIVITY (1643)
CHRONIC MYELOID, POLYCYTHEMIA,
PHILADELPHIA CHROMOSOME (0010)
CHRONIC MYELOLEUKEMIA, CYTOGENETICS
(2574)*
CLOSTRIDIA, IMMUNOSUPPRESSION, REVIEW
(1286)*
CNS, CHILDREN, INCIDENCE (0283)
COW LYMPHOCYTES, BOVINE LYMPHOCYTOSIS,
C-TYPE VIRUS PARTICLES (1877)
DETECTION, COMPLEMENT BINDING, VIRUS
(0711)
DIABETES, DNA SYNTHESIS, GLUCOSE
METABOLISM (0775)
7,12-DIMETHYLBENZ(A)ANTHRACENE, BONE
MARROW CHROMOSOME (0061)
DNA, 5-METHYLCYTOSINE, HUMAN (2530)
DOG BITE, CHILDHOOD (2133)
DOMESTIC ANIMALS, VIRAL ETIOLOGY,
REVIEW (0389)*
EMBRYO CELL CULTURE, THYMUS CELL
CULTURE, MOUSE (0599)
EPSTEIN-BARR VIRUS, HUMAN EMBRYONIC
CELL LINE (0570)
FAMILIAL (2576)*
FAMILY G, INCIDENCE, COLON (2533)
FELINE, VIRUS (1894)
FELINE, VIRUS, GROUP-SPECIFIC ANTIGEN (1977)

FRIEND VIRUS, COMPLEMENT FIXATION,
MOUSE (2456)
FRIEND VIRUS, ERYTHROID DIFFERENTIA-
TION (0603)
FRIEND VIRUS, SPLEEN (1022)
FRIEND VIRUS, SPLEEN PARABIOSIS (14)
GASTRIC AND LUNG CANCER, VIRUS-LIKE
PARTICLES, VIRUS (1414)
GENETIC FACTORY, DERMATOGLYPHIC
PATTERNS (0363)
GENETIC IMPLICATION, TWIN, HUMAN
(0364)
GENETIC SUSCEPTIBILITY, GROSS VIRUS,
THYMUS GRAFT (0172)
GLYCOLIPID, LEUKOCYTE, HUMAN (2563)
GRAFFI VIRUS, MYELOGENOUS, MICE (10)
GROSS VIRUS, BITTNER VIRUS, MAMMARY
GLAND TUMOR, MOUSE (1928)
GROSS VIRUS, CHROMOSOMES, MICE (1904)
GROSS VIRUS, IMMUNOLOGY, GENETICS
(1970)
GROWTH STAGES, ANTIBODY, L1210, MICE
(2448)
GUINEA PIG, VIRUS (1039)
HAPTOGLOBIN TYPES (2023)*
HEMADSORPTION REACTION, FELINE, HUMA
(1976)
HEMATOPOETIC CANCER, DEATH RATES,
EPIDEMIOLOGY (0761)
HERPES-LIKE VIRUS, GUINEA PIG (1920)
HISTONES, INHIBITION, RNA SYNTHESIS,
HUMAN (2515)
HL-A ANTIGEN FREQUENCIES (0714)
HODGKIN'S DISEASE, RESISTANCE, CANDI
ALBICANS (2461)
HUMAN, LEUKOCYTIC LEUKEMIA VIRUS,
MORPHOLOGY (1418)
HUMAN, MYELOMONOCYTIC, BONE MARROW,
MICROCHROMOSOMES (1147)
HUMAN LEUKEMIC CELLS, EPSTEIN-BARR
VIRUS (1882)
HUMAN LYMPHOID, BLOOD LYMPHOCYTE CEL
MEMBRANE, ULTRASTRUCTURE OF ACID
CARBOHYDRATES (2142)*
HUMAN PERIPHERAL BLOOD, HERPES TYPE
VIRUS (1925)
HYDROGEN TRANSPORT, BONE MARROW, HUM
(2060)
IMMUNE LYMPHOCYTES, VIRUS ANTIGEN,
SUPPRESSION OF TUMOR GROWTH (1969)
IMMUNOFLUORESCENCE, PARABLASTS,
CHILDREN, CONTACT PERSONS (0712)
IMMUNOFLUORESCENCE MICROSCOPY, BONE
MARROW, CHILDREN (0233)
INCIDENCE, BACILLUS CALMETTE-GUERIN,
INOCULATION OF BACILLUS (1250)
INCIDENCE, JAPAN, ATOMIC BOMB
SURVIVORS (1398)
INCIDENCE AMONG DOGS, LYMPHOSARCOMA
(2039)
INCIDENCE IN KENYA (1166)
INCIDENCE IN WEST GERMAN ARMY (1613)
INCREASED ERYTHROID MITOSES, CHROMO-
SOME ABNORMALITIES, HUMAN (1686)
INDUCTION, HUMAN LEUKEMIC CELLS,
MONKEYS (1867)
INDUCTION, STRONTIUM 90, X-IRRADIATIO
(1839)

INDUCTION IN MICE, HUMAN LYMPHOMA
 CELLS, LATENCY (2136)
 INFECTIOUS MONONUCLEOSIS, BURKITT'S
 LYMPHOMA, CELL POPULATION (2494)
 INHERITED DISEASES, CHROMOSOMAL
 BREAKAGE (0856)
 INTERFERON, POLYINOSINIC-POLYCYTIDYLIC
 ACID, FIBROBLASTS (1528)
 LEUKOCYTES, INTERFERON PRODUCTION
 (0335)*
 LEUKEMOGENESIS, AEROSOL EXPOSURE,
 VIRUS, RAUSCHER MURINE LEUKEMIA
 VIRUS (0608)
 LEUKEMOGENESIS, 7,12-DIMETHYLBENZ(A)
 ANTHRACENE, PHORBOL (0893)
 LEUKEMOGENIC VIRUS, GUINEA PIG (1871)
 LOW-LEUKEMIC STRAIN MICE, MURINE
 LEUKEMIA VIRUS, ANTIGEN (0596)
 LYMPHOBLAST, TRANSFER RNA SPECIES,
 AMINOACYLATION (0790)
 LYMPHOBLAST, TRNA (1204)
 LYMPHOBLASTIC, ACID DNASE, CYTOTOXIC
 EFFECT, MICE (1041)
 LYMPHOBLASTIC, LACTATE DEHYDROGENASE,
 ISOCITRATE DEHYDROGENASE, LIVER,
 SPLEEN, BURSA (1644)
 LYMPHOCYTIC, ANTILYMPHOCYTE SERUM,
 MURINE VIRUS (1543)
 LYMPHOCYTIC, TRYPTOPHANYL TRANSFER
 RNA SYNTHETASE, HUMAN (2510)
 LYMPHOID, AKR-A CULTURE, GROSS
 LEUKEMIA VIRUS, MOUSE (0171)
 LYMPHOID, BENZENE, OCCUPATIONAL HAZARD
 (1370)
 LYMPHOMA, IMMUNOLOGICAL ABNORMALITIES,
 SIBLING GROUP (1123)
 LYMPHOMA, PHENYLALANINE TRANSFER RNA,
 HUMAN (2520)
 LYMPHOMA, VIRUS-LIKE PARTICLES, HUMAN
 (0569)
 LYMPHOSARCOMA, VIRUS PARTICLES (0550)
 MAMMARY TUMORS, C-TYPE VIRUS
 PARTICLES, RAT (1870)
 MAST CELL, TRANSPLANTATION OF TUMOR,
 CANINE (2131)
 MAZURENKO VIRUS, SPECIES SPECIFICITY,
 DOG, MOUSE (2319)
 MOLONEY LEUKEMIA VIRUS, PREDNISOLONE,
 THYMUS (0173)
 MOLONEY VIRUS, C-TYPE PARTICLES (1447)
 MOLONEY VIRUS, TRANSMISSION, CHROMO-
 SOME (1905)
 MONOCYTIC, MYELO-MONOCYTIC, ULTRA-
 STRUCTURE, HUMAN (2115)
 MORTALITY, BACILLUS CALMETTE-GUERIN
 VACCINATION, SCOTLAND (1251)
 MORTALITY, BAVARIA (0270)
 MOUSE LEUKEMIA CELLS, ALLOGRAFT
 SURVIVAL, X-IRRADIATION (0225)
 MOUSE LEUKEMIA VIRUS, IMMUNOTHERAPY,
 ETIOLOGY, MONONUCLEOSIS (1738)
 MURINE, GROSS VIRUS, ANTIGEN (1523)
 MURINE, POLYAMINE ACCUMULATION,
 SPERMIDINE AND PUTRESCINE SYNTHESIS
 (2074)
 MURINE, VIRAL ANTIGENS, DETECTION
 (2413)
 MURINE LEUKEMIA-ASSOCIATED ANTIGEN,

ANTIGENIC ANALYSIS, L STRAIN MOUSE
 CELLS (0165)
 MURINE LEUKEMIC TISSUES, INTRACISTER-
 NAL VIRAL PARTICLES (1442)
 MYCOTOXINS, TUMOR, MICE (1776)
 MYELOBLASTIC, DNA, CHROMOSOME, HUMAN
 (2564)
 MYELOGENOUS, MULTIPLE MYELOMA, EPSTEIN
 BARR VIRUS, CELL SURFACE (1433)
 MYELOGENOUS GRANULOCYTIC, N-NITRO-
 SOBURYLUREA, ASCITES TUMOR (1353)
 MYELOID, CHROMOSOME ANOMALIES,
 CHRONIC, ACUTE, PHILADELPHIA CHROMO-
 SOME (1280)
 MYELOID, PHILADELPHIA CHROMOSOME,
 Y CHROMOSOME, CASE REPORT (1721)*
 MYELOMONOCYTIC, CHRONIC LYMPHOCYTIC,
 CHLORAMBUCIL (1365)
 MYELOMONOCYTIC, FANCONI'S ANEMIA,
 CHROMOSOME, VIRUS (0150)
 MYELOPROLIFERATIVE DISEASE, ABNORMAL
 CYTOLOGY (1146)
 N-NITROBUTYLUREA (0091)
 N-(4-(5-NITRO-2-FURYL)-2-THIAZOLYL)
 ACETAMIDE, STOMACH NEOPLASM (0417)
 N-NITROSOBUTYLUREA, MAMMARY TUMOR,
 MICE, RATS (0092)
 NUCLEIC ACIDS, RNA, DNA (1431)
 OCCUPATIONAL EXPOSURE TO BENZENE,
 ATOMIC BOMB IRRADIATION (1399)
 ONCOGENIC VIRUSES, PRECIPITATING
 FACTORS (0351)
 PAPOVA VIRUS, HAMSTER, LIVER, THYMUS
 (0672)
 PHAGOCYTOSIS, IODINE, HUMAN (2063)
 PHILADELPHIA CHROMOSOME (1753)*
 PLASMOCYTIC, CHROMOSOMAL ANOMALIES,
 CASE REPORT (1713)*
 RADIATION, BONE MARROW AUTOTRANSPLANT,
 MOUSE (1864)*
 RADIATION, THERAPEUTIC DOSE (0370)
 RADIATION VIRUS, IMMUNIZATION (1968)
 RAUSCHER LEUKEMIA VIRUS, CHANGES IN
 ENZYME ACTIVITY (1907)
 RAUSCHER VIRUS, ANTIGEN SUBUNITS,
 HEMAGGLUTINATION-INHIBITION ASSAY
 (2409)
 RAUSCHER VIRUS, FREUND ADJUVANT, MOUSE
 (2323)
 REGRESSION, VIRUS, FRIEND, MICE (2313)
 RETICULOENDOTHELIOSIS, DISTRIBUTION
 OF CELLS IN TISSUES, NEOPLASTIC CELL
 (1240)
 RNA, DNA POLYMERASE (0792)
 RNA, DNA, SYNTHESIS, POLYMERASE (1641)
 SARCOMA, RADIONUCLIDES, REVIEW (1274)
 SARCOMA VIRUS, C-TYPE MOUSE MAMMARY
 TUMOR VIRUS, B-TYPE POLYMERASE
 (0589)
 SEX MORTALITY RATIO, EPIDEMIOLOGY
 (0275)
 SOLID TUMOR, MORTALITY, INCIDENCE IN
 TWINS (1606)
 SPLENECTOMY, MOUSE (2552)
 SPONTANEOUS, FISCHER RAT, PATHOLOGY
 (0323)
 SQUAMOUS CELL CARCINOMA, 3-METHYL-
 CHOLANTHRENE, MICE (0949)

STRONTIUM 90, MYELOID NEOPLASMS IN SWINE (1841)
 STRONTIUM 90, X-IRRADIATION (1839)
 STRONTIUM 90 RADIATION, MOUSE (2285)
 TRANSFORMATION, NORMAL MARROW CELL GRAFT (1201)
 TRANSPLANT, NORMAL TISSUE RNA, IMMUNO-SUPPRESSION, MOUSE (1557)
 TRNA, EMBRYONIC TISSUE (2503)
 TUMOR ISOLATES, MYCOBACTERIA (2125)
 TUMORS, IMMUNITY (2159)
 VIRAL, MYELOID, STAPHYLOCOCCUS, CHICK (1889)
 VIRAL ETIOLOGY, MAN, REVIEW (0867)*
 VIRUS, ANTIGENICITY, HUMAN CELLS, ANIMAL CELLS (2295)
 VIRUS, GROUPS SPECIFIC ANTIGEN, FELINE (1975)
 VIRUS, MAGNESIUM ACETATE, MANGANESE ACETATE (1037)
 VIRUS, MOUSE SPLEEN, WHOLE BODY IRRADIATION (0592)
 VIRUS, MURINE SARCOMA, RNA (1076)
 VIRUS, SPREAD, BIRD (2166)*
 VIRUS PARTICLES IN GUINEA PIG, TRANSMISSION (1865)
 VIRUS-LIKE PARTICLES, BONE MARROW CELLS, HERPES SIMPLEX VIRUS (0149)
 X-IRRADIATION, CHILDHOOD CANCER (1605)
 X-RAY RADIATION, HYDROCORTISONE, MICE (0999)

LEUKOCYTE

ADENINE PHOSPHORIBOSYLTRANSFERASE, HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE (2083)
 ATYPICAL LYMPHOID CELLS, PRELYMPHOMATOUS CONDITION, SEZARY SYNDROME (1206)
 CARCINOMA, MIGRATION INHIBITION (2452)
 CHROMOSOME ABERRATIONS, NEUTRON IRRADIATION, PIG (1005)
 CHROMOSOME ABERRATIONS, X-IRRADIATION THERAPY, IN UTERO (0538)
 CLONED HUMAN, EPSTEIN-BARR VIRUS ANTIGEN (1021)
 CYCLOHEXYLAMINE, MUTAGENESIS, HUMAN (2203)
 HERPES-LIKE VIRUS, INFECTION, GUINEA PIG (2335)
 HUMAN, METAPHASE DEFECTS, L-CYSTEINE, PROTECTIVE ACTION (1360)
 HUMAN PERIPHERAL BLOOD, LEUKEMIA, HERPES TYPE VIRUS (1925)
 INTERFERON PRODUCTION, LEUKEMIA (0335)*
 LEUKEMIA, GLYCOLIPID, HUMAN (2563)
 LEUKOCYTIC ZINC CONTENT, SKIN NEOPLASIA (0787)
 LITHIUM TREATMENT, MANIC DEPRESSIVE SYNDROME (1835)
 MIGRATION INHIBITOR, HUMAN TUMORS, IMMUNITY (1545)
 PHENOTYPE, HODGKIN'S DISEASE, HL-A ANTIGEN (0717)

LEUKOPLAKIA

LYMPHOCYTES, ORAL MUCOSA (1150)
 URETRAL CALCULUS (2141)*

LEUKOSIS

AVIAN, COMPLEMENT FIXING ANTIGEN, ROUS SARCOMA VIRUS (1966)
 BOVINE, SWEDEN, LYMPHOCYTOSIS (2130)
 COINCIDENCE IN CATTLE HERDS, BOVINE LYMPHOCYTOSIS (2128)
 COMPARISON, BOVINE LEUKOTIC VIRUS-LIKE PARTICLES, FELINE LEUKOSIS VIRUS (1874)
 HUMAN AND BOVINE, INCIDENCE IN BALTIC U.S.S.R. (2048)
 IMMUNOGLOBULIN, SPLEEN AND LYMPH NODE IGM, BOVINE (2013)
 RNA, AVIAN VIRUS (1887)

LIMONENE

DIBENZOPYRENE, TRICAPRYLIN, ADENOMA, MOUSE (1795)

LIP

CANCER, INCIDENCE IN CONNECTICUT (1612)
 MUCOSA, CANCER, 7,12-DIMETHYLBENZ(A) ANTHRACENE, HAMSTER (0453)

LIPID

ALTERED, NEWT TEST, NECROSIS (0036)
 CARCINOMA MORTALITY, POLYUNSATURATED FAT-RICH DIET (1363)
 COMPOSITION, N-2-FLUORENYLACETAMIDE, LIVER PLASMA MEMBRANES (1305)
 ESSENTIAL FATTY ACIDS, WHOLE BLOOD, EHRLICH ASCITES CARCINOMA, SARCOMA 180 (1655)
 FATTY TISSUE, MAMMARY TUMOR, SURFACE MOTILITY, PHAGOCYTOSIS (1679)
 GLYCOLIPID, SV40, POLYOMA VIRUS, FIBROBLASTS (1102)
 GLYCOLIPID, TRANSFORMED CELL, HAMSTER (2477)
 LECITHIN, CHOLESTEROL, 3-METHYL-CHOLANTHRENE (1338)
 LIVER, NEOPLASMS, HUMAN (2058)
 PROTEOLIPID, WALKER RAT SARCOMA, ISOLATION (2068)
 SERUM, MYELOMA, IMMUNOGLOBULINS, MAN (2445)

LIPOGRANULOMA

HUMAN LIVER BIOPSY, FATTY CHANGE IN LIVER (2102)
 SCLEROSING, PARAFFINOMA, MINERAL OIL INJECTIONS (1860)

LIPOMA

CHLORPROPAMIDE (1830)

LIPOPROTEIN

SERUM, HIGH-DENSITY LEVEL (0785)

LIPOSARCOMA

METHYLCHOLANTHRENE, IMMUNOTHERAPY, GUINEA PIG (1984)
 RNA-TRANSFERRED IMMUNITY, 3-METHYL-CHOLANTHRENE (0077)

LITHIUM

MANIC DEPRESSIVE SYNDROME, BLOOD LEUKOCYTES (1835)

LIVER

2-ACETYLAMINOFLUORENE, ANTIGEN, RAT (2426)
 2-ACETYLAMINOFLUORENE, METABOLITE BINDING, NUCLEIC ACIDS, RAT (1301)
 N-ACETYLATION, HEPATOMA HISTONE, RAT (2056)

AFLATOXIN, CYTOPLASM, ENDOPLASMIC RETICULUM, MITOCHONDRIA, RATS (1780)
 AFLATOXIN, SUBACUTE CHANGES, BEAGLE (1778)
 AFLATOXIN B, NUCLEAR RNA, RNA POLYMERASE, RAT (0046)
 AFLATOXIN B1, CARCINOMA, HEPATECTOMY, RAT (2210)
 2-AMINO-N-ACETYLFUORENE, CARCINOMA, PORPHYRINS, RAT (2190)
 ANTIBODY, PHAGOCYTOSIS, LEUKEMIA, SPLEEN, 7,12-DIMETHYLBENZ(A)ANTHRACENE (1451)
 ANTIGENS, HEPATOMA, DIMETHYLAMINO-AZOBENZENE, DIETHYLAMINOAZOBENZENE (0434)
 AZO DYE BINDING, N-METHYL-4-AMINO-AZOBENZENE (0056)
 BENZOPYRENE, CARBON MONOXIDE, RAT (0459)
 BINDING, ORTHO-AMINOAZOTOLUENE, REGENERATION (1320)
 BIOSYNTHESIS OF BILE ACIDS, METHYL-CHOLANTHRENE (0462)
 BLOOD, LUNG, 4-HYDROXYAMINOQUINOLINE-1-OXIDE (1358)
 CANCER, BANTU, CARCINOGENIC MYCOTOXIN (2135)
 CANCER, BEDOUINS IN ISRAEL, PATHOLOGY AND EPIDEMIOLOGY (1168)
 CANCER, CHINESE-BORN POPULATION OF SINGAPORE (1165)
 CANCER, STEROIDS, RATS, LEYDIG CELLS, HYPOTHALAMUS (1313)
 CARBOHYDRATE METABOLISM, AFLATOXIN B1, CHICK (1311)
 CARCINOGENS, PROTEIN SYNTHESIS (2151)
 CARCINOMA, AFLATOXIN CONSUMPTION, SWAZILAND (1781)
 CARCINOMA, BLOOD MALIGNANCIES, MYCOTOXINS (1276)
 CARCINOMA, CIRRHOSIS, AFLATOXIN, RAT (2206)
 CARCINOMA, CIRRHOSIS, IMMUNOGLOBULIN (0232)
 CARCINOMA, ALPHA-FETOPROTEIN (2003)
 CARCINOMA, ALPHA-FETOPROTEIN, GI CANCER, CARCINOEMBRYONIC ANTIGEN (0240)*
 CARCINOMA, HODGKIN'S DISEASE (1718)*
 CARCINOMA, 4-NITROQUINOLINE-1-OXIDE, TRANSPLANTABLE TUMOR LINE, RAT (1824)
 CARCINOMA, RAT, N-HYDROXY-N-2-FLUORENYLACETAMIDE (0409)
 CELL, METAPHASE CHROMOSOME ABERRATIONS, COBALT 60, HAMSTER (1394)
 CELL, NUCLEAR MEMBRANE PERMEABILITY, DIETHYLNITROSAMINE, RAT (0084)
 CELL CULTURE, AFLATOXIN B1, INHIBITION OF RNA SYNTHESIS (0914)
 CELL NUCLEI RNA POLYMERASE, N,N-DIMETHYL-4-AMINOAZOBENZENE, RAT (1783)
 CELL PROLIFERATION, RATS, HOMEOSTATIC REGULATION (1350)
 CELL REGENERATION, MITOTIC RATES, 4-DIMETHYLAMINOAZOBENZENE (1782)
 CHICK EMBRYOS, PALMOTOXINS, AFLATOXIN (0425)
 CHROMATIN PROTEINS, 3-METHYLCHOLANTHRENE, NA C1-EXTRACTABLE, RAT (1337)
 CHROMATIN TEMPLATE ACTIVITY, 3-METHYL-CHOLANTHRENE (0071)
 CHROMOSOMES, THIOACETAMIDE (1297)
 CIRRHOSIS, CORTISONE THERAPY, CANCER (1163)*
 CIRRHOSIS, DIET, HEPATOCARCINOMA, RAT (2471)
 CIRRHOSIS, TUMOR, PATHOGENESIS (1598)*
 CREATINE KINASE, CARBON TETRACHLORIDE, CARCINOGENESIS, MOUSE (1288)
 CULTURE, 4-NITROQUINOLINE-1-OXIDE, ULTRASTRUCTURE, RAT (0094)
 CYCASIN, DIET, HUMAN (2490)
 CYTOCHROME P-450, 3-METHYLCHOLANTHRENE PHENOBARBITAL, RAT (0464)
 DIETHYLNITROSAMINE, CYCLOHEXIMIDE, RAT (1372)*
 DIETHYLNITROSAMINE, HEPATECTOMY, RAT (0959)
 DIETHYLNITROSAMINE, PARTIAL HEPATECTOMY, RENAL TUMORS (1812)
 DIETHYLNITROSAMINE, SORBITOL DEHYDROGENASE, RAT (0085)
 DIETHYLNITROSAMINE CARCINOGENESIS, ENZYMES, RAT (0960)
 DIETHYLSTILBESTEROL, LYSYL-TRANSFER RNA, CHICKEN (1205)
 DIMETHYLAMINOAZOBENZENE, CARCINOGENESIS, NAPHTHYLSIOTHIOCYANATE INHIBITION, RAT (0433)
 P-DIMETHYLAMINOAZOBENZENE, ENZYME ACTIVITY IN RAT (0922)
 P-DIMETHYLAMINOAZOBENZENE, SYNESTROL, TESTOSTERONE, RAT (1314)
 7,12-DIMETHYLBENZ(A)ANTHRACENE, DNA BINDING, RAT (2224)
 7,12-DIMETHYLBENZ(A)ANTHRACENE, HEPATECTOMY, RAT (2218)
 DIMETHYLNITROSAMINE, MOUSE (2246)
 P-DIMETHYLPHENYLAZODIBENZOTHIOPHENE, CARCINOGENICITY, RAT (0924)
 DNA, ASCITES TUMOR, ORTHOPHOSPHATE, THYMIDINE (1648)
 ENVIRONMENTAL CONTAMINANTS, MICROSOMAL ENZYMES (0848)
 ENZYME ACTIVITY, CITRIC ACID CYCLE, AFLATOXIN (0920)
 ENZYMES, TRANSFER RNA, ETHIONINE (2146)
 ETHIONINE NODULES, ULTRASTRUCTURES, RAT (1296)
 FAMILIAL HEPATOMA, HEPATITIS-ASSOCIATED ANTIGEN (1712)*
 FATTY CHANGE, LIPOGRANULOMA, HUMAN (2102)
 FERRITIN, CARCINOGENS, RAT (0475)
 ALPHA-FETOPROTEIN, AGE CORRELATION (0231)
 N-2-FLUORENYLACETAMIDE, HYPERPLASTIC HEPATIC NODULES (1299)
 GAMMA RADIATION, ALPHA-AMINOISOBUTYRIC ACID, RAT (1386)
 GLUCOSE-6-PHOSPHATASE, HORMONE, DIETHYLNITROSAMINE (1814)

GLYCOGENOSIS, HEPATOMAS, ULTRASTRUCTURE, HUMAN (2073)
 HAMSTER FIBROSARCOMA, SV40, ARGINASE (1496)
 HEMANGIOSARCOMA, DIMETHYLNITROSAMINE, LUNG ADENOMA (0080)
 HEPATIC CANCER, MYCOTOXIN NUCLEIC ACID SYNTHESIS, FOOD (0849)
 HEPATOCARCINOGENESIS, 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE, CHLORAMPHENICOL, RAT (1316)
 HEPATOCARCINOMA, 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE, RAT (0429)
 HEPATOCARCINOMA, MONKEY, ULTRASTRUCTURE, N-NITROSODIETHYLAMINE (0955)
 HEPATOCARCINOMA, SENEIO LONGILOBUS (1293)
 HEPATOCELLULAR CARCINOMA, HEPATITIS-ASSOCIATED ANTIGEN (0723)
 HEPATOCELLULAR CARCINOMA, STERIGMATOCYSTIN, RATS (0402)
 HEPATOCELLULAR CHANGES, GLYCOGEN, N-NITROSOMORPHOLINE (1818)
 HEPATOMA, AZO DYE, ULTRASTRUCTURE, RAT (1785)
 HEPATOMA, CHROMATIN, RNA, RAT (2198)
 HEPATOMA, COLONY INHIBITION, IMMUNE LYMPH NODES, RAT (1550)
 HEPATOMA, DNA, CHROMOSOMES (1691)
 HEPATOMA, ETHANOLAMINE, CHOLINE (1660)
 HEPATOMA, N,N'-2,7-FLUORENYLENE-BISACETAMIDE, X-IRRADIATION (0040)
 HEPATOMA, GROWTH RATE, HEXOKINASE (0288)
 HEPATOMA, MITOCHONDRIAL MEMBRANE PROTEINS, RAT (1652)
 HEPATOMA, BETA-PROIOLACTONE, TUMOR INDUCTION (0399)
 HEPATOMA, REGENERATION, URETHAN, MOUSE (0971)
 HEPATOMA, RNA, SUBRIBOSOMAL PARTICLES (1636)
 HEPATOMA, STAGES IN MALIGNANT TRANSFORMATION, DIETHYLNITROSAMINE (0957)
 HEPATOMA, TUMOR IMMUNITY, GUINEA PIG (1992)
 N-HYDROXY-N-ACETYL-4-AMINOBIIPHENYL, NUCLEIC ACIDS, RAT (2181)
 HYPERPLASTIC NODULE, RAT, 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE, 2-FLUORENYL ACETAMIDE, DL-ETHIONINE (0430)
 IMMUNOSUPPRESSORS, RATS, DIETHYLNITROSAMINE (1815)
 IN VITRO MALIGNANT TRANSFORMATION, AFLATOXIN B₁, RAT (1312)
 IRRADIATION, AMINO ACIDS, PERFUSION (0537)
 KIDNEYS, X-IRRADIATION, AUTORADIOGRAPHY, MICE (2279)
 KUPFFER CELL, BILE DUCT EPITHELIUM, HYPERPLASIA, AFLATOXIN B₁, HAMSTER (0517)*
 LESIONS, CARBON TETRACHLORIDE, 3-METHYLCHOLANTHRENE (0945)
 LIPIDS, NEOPLASMS, HUMAN (2058)
 LIPOTROPE-DEFICIENT DIET, AFLATOXIN CARCINOGENESIS (0915)
 LUNG, CARCINOMA, HYDRAZINE SULFATE, MOUSE, ISONIAZIDE METABOLISM, MAN (0415)
 LUNG, MONURON CARCINOGENICITY, RAT, MOUSE (0897)
 LYSOSOMAL ENZYME ACTIVITY, RENAL CARCINOMA (1645)
 LYSOSOMES, 4-DIMETHYLAMINOAZOBENZENE, LYSOSOMAL ACTIVITY, RAT (1784)
 MAMMARY TUMOR VIRUS, BRAIN GR MOUSE (0629)
 METABOLISM, DEGRADATION PRODUCTS, AFLATOXINS (0917)
 7-METHYLBENZ(A)ANTHRACENE METABOLISM, ADRENAL, 7,12-DIMETHYLBENZ(A)-ANTHRACENE (0066)
 3-METHYLCHOLANTHRENE, DIMETHYLNITROSAMINE DEMETHYLASE INHIBITION, RAT (0466)
 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE, BINDING, RAT (2211)
 DIETARY INDUCTION OF ENZYMES (0052)
 3-METHYLCHOLANTHRENE, RAT (1786)
 MICROSOMAL MEMBRANE, NUCLEIC ACID, CHEMICAL CARCINOGEN, RAT (0913)
 MICROSOME, FOWL, REPTILE, AFLATOXIN B₁ METABOLISM (1309)
 MITOCHONDRIA, MELANOMA, AMINO ACIDS, HAMSTER (2546)
 MITOCHONDRIA, PHOSPHORYLATION, ETHIONINE, S-ETHYL-L-CYSTEINE, RAT (2192)
 MITOTIC RATES, 4-DIMETHYLAMINO-AZOBENZENE, REGENERATION (1782)
 MOUSE HEPATOMA, NUCLEAR ATPASE LOCALIZATION (0259)
 N-NITROSODIMETHYLAMINE, TUMORIGENESIS, MASTOMYS (0958)
 NITROSOHEXAMETHYLENAMINE, ULTRASTRUCTURAL STUDY, RAT (1817)
 NORMAL, HEPATOMA, GROWTH INHIBITOR, RAT (2072)
 NOVIKOFF ASCITES HEPATOMA CELLS, CYTOPLASMIC GLYCOGEN FOCI, GLUCOSE INCORPORATION, (2061)
 NUCLEIC ACID METHYLATION, DIMETHYLNITROSAMINE, METABOLISM (0473)
 OLEIC ACID, LINOLEIC ACID, STEARIC ACID, MALIGNANT NEOPLASMS (1639)
 ORTHOAMINOAZOTOLUENE, BIOMYCIN, MOUSE (0025)
 PHENOBARBITAL, 3-METHYLCHOLANTHRENE, RAT (2237)
 PHOSPHOFRUCTOKINASE, P-DIMETHYLAMINO-AZOBENZENE, RAT (1318)
 PLASMA MEMBRANES, LIPID COMPOSITION, N-2-FLUORENYLACETAMIDE (1305)
 POLYRIBOSOMES, X-IRRADIATION, HORMONE RAT (0544)
 PRIMARY CANCER, AUSTRALIA ANTIGEN (0724)
 PRIMARY CANCER, CIRRHOSIS, GIANT CELL HEPATITIS, INFANT (2032)*
 PRIMARY CANCER, ALPHA-FETOPROTEINS, LOCALIZATION, HUMAN (2004)
 PROTEIN, P-DIMETHYLAMINOAZOBENZENE, BINDING, MICE AND HAMSTERS (0923)
 PROTEIN ADDUCT, N-HYDROXY-2-FLUORENYLACETAMIDE, RAT (0407)

RAT HEPATOMA CELLS, TYROSINE AMINO-
 TRANSFERASE, 5-BROMODEOXYURIDINE
 (2078)
 REGENERATION, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, NUCLEIC ACID SYNTHESIS
 (0058)
 RHESUS MONKEY, DIETARY AFLATOXINS
 (0426)
 RNA METABOLISM, THIOACETAMIDE, RAT
 (1775)
 SPLEEN, SCHISTOSOMIASIS, FOLLICULAR
 LYMPHOMA (2122)
 SYNCARCINOGENESIS, NITROSAMINES, RATS
 (0435)
 SYNGENIC CELLS, 3-METHYLCHOLANTHRENE,
 TUMOR INHIBITION (0079)
 THIOACETAMIDE, TUMORS, MICE (0969)
 THOROTRAST, CIRRHOSIS, CARCINOMA,
 HUMAN (1397)
 THOROTRAST, TUMORS (0366)
 TRANSFER RNA, MORRIS HEPATOMA, OVA
 (2526)
 TRNA, MORRIS 5123 HEPATOMA (2025)
 TUMOR, 4-AMINOAZOBENZENE DERIVATIVES,
 TARGET ORGANS, DOSE EFFECT, RAT
 (0055)
 TUMOR, CYCASIN, PULMONARY TUMORS
 (0895)
 TUMOR, ETHYL-ALPHA-P-CHLOROPHENOXYISO-
 BUTYRATE, LIVER CATALASE, RAT (2114)
 TUMOR, METABOLIC CHANGES, THIOACETA-
 MIDE (0970)
 TUMOR, 3'-METHYL-4-DIMETHYLAMINO-
 AZOBENZENE, SOLUBLE MACROMOLECULES,
 RAT (1317)
 TUMOR, NEWBORN AND ADULT HAMSTERS,
 CYCASIN (1765)
 239PU EXPOSURE, SPECULATIVE ESTIMATE
 OF HAZARD, TUMOR RISK (1003)
 ULTRASTRUCTURE, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, DIMETHYLNITROSAMINE
 (0081)
 UREA CYCLE ENZYMES, ARGINASE, EHRlich
 ASCITES TUMOR (2067)
 VIRUS PARTICLES, FIBROBLASTS (1413)
 ADENOCARCINOMA, NITROSAMINE, MOUSE
 (2239)
 ADENOMA, ALUMINUM, 4-NITROQUINOLINE
 1-OXIDE (0096)
 ADENOMA, BENZO(A)PYRENE HYDROXYLASE
 ACTIVITY, FLAVONE INDUCER (0070)
 ADENOMA, BIS(CHLOROMETHYL) ETHER,
 CHRONIC INHALATION, MICE (1761)
 ADENOMA, CARCINOMA, HYDRAZINE SULFATE,
 GONAECTOMY, MOUSE (0414)
 ADENOMA, LEUKEMIA, N-DIAZOACETYL-
 GLYCINAMIDE, N-DIAZOACETYLGLYCINE
 HYDRAZIDE, MOUSE (0401)
 ADENOMA, LIVER HEMANGIOSARCOMA,
 DIMETHYLNITROSAMINE (0080)
 ADENOMA, METHOTREXATE, CYCLO-
 PHOSPHAMIDE, MOUSE (2185)
 ADENOMA, NITROSAMINE, SODIUM NITRITE,
 MOUSE (2241)
 ADENOMA, RETICULOSARCOMA, AMYLOIDOSIS,
 7-HYDROXYTHEOPHYLLINE (1764)
 ADENOMA, THYMECTOMY, MICE (2430)

ADENOMA, TRANSPLACENTAL EFFECT,
 DIETHYLNITROSAMINE, MOUSE (1816)
 ADENOMA, URETHAN, RADIATION (0101)
 ALVEOLAR CELL CARCINOMA, DNA, ALVEOLAR
 MACROPHAGE (0736)
 ALVEOLAR EPITHELIAL CELLS, 4-NITRO-
 QUINOLINE 1-OXIDE, NUCLEOLAR ALTERA-
 TIONS (0491)
 ALVEOLI, PLUTONIUM AEROSOL, RAT (1843)
 AMYLOID DEPOSITS, OAT-CELL CARCINOMA,
 MORPHOLOGY (1664)
 BENZO(A)PYRENE, PREGNANT MICE,
 PROGENY, PULMONARY ADENOMA (1332)
 BENZO(A)PYRENE, RATS, METABOLISM
 (0936)
 BENZO(A)PYRENE, UPTAKE, HAMSTER (2229)
 BRONCHIAL CANCER, PLEURAL MESOTHELIOMA
 ASBESTOS EXPOSURE (1610)
 BRONCHIAL CARCINOMA, CIGARETTE SMOK-
 ING, BEAGLE (0108)
 BRONCHIAL CARCINOMA, GONADOTROPHIN
 SECRETION, TROPHOBLASTIC DIFFEREN-
 TIATION (0774)
 BRONCHIAL CARCINOMA, HYDROCARBONS,
 CARCINOGENS, AIR POLLUTION (0461)
 BRONCHIAL EPITHELIUM, DRY WEIGHT AND
 HYDRATION CHANGES, CO 60-GAMMA
 IRRADIATION (1850)
 BRONCHIAL SECRETION, CARCINOMA,
 TOBACCO SMOKE (0750)
 BRONCHIOLO-ALVEOLAR TUMORS, FILTERED
 CIGARETTES, DOGS (0973), (0974)
 BRONCHOALVEOLAR CANCER, OVINE PULMON-
 ARY ADENOMATOSIS, NEOPLASTIC
 FEATURES (0820)
 BRONCHOALVEOLAR CARCINOMA, PULMONARY
 ADENOMATOUS CHANGE (2139)
 BRONCHOGENIC CARCINOMA, HISTOPATHOLOGY
 GROWTH RATE, METASTASIS (0764)
 BRONCHOGENIC CARCINOMA, TUMOR GROWTH,
 RISK (1628)
 BRONCHUS, CARCINOMA, ETIOLOGY, REVIEW
 (0872)*
 CANCER, AIR POLLUTION, EPIDEMIOLOGY
 (0016)
 CANCER, BERYLLIUM EXPOSURE (0300)*
 CANCER, CIGARETTE SMOKING,
 EPIDEMIOLOGY (0286)
 CANCER, CYCLAMATE, HEPATOMA, MOUSE,
 REVIEW (0378)*
 CANCER, EPIDEMIOLOGY, TOBACCO (1741)
 CANCER, EPIDEMIOLOGY, URBAN AREA
 (2482)
 CANCER, FINLAND, TUBERCULOSIS (2117)
 CANCER, GOLDEN HAMSTERS, DIETHYL-
 NITROSAMINE, ORGANOTROPY (1345)
 CANCER, HEMATITE MINING (0015)
 CANCER, HIGH-RISK GROUPS, CIGARETTE
 SMOKING (0751)
 CANCER, HISTOLOGY, MORPHOLOGY (0829)*
 CANCER, INCIDENCE, AIR POLLUTION,
 SMOKING, ITALY (0383)*
 CANCER, INFLUENZA VIRUS, MICE, CELL
 METAPLASIA (0564)
 CANCER, MORTALITY RATES, SMOKING
 (0017)
 CANCER, NICKEL, COBALT, OCCUPATIONAL
 EXPOSURE (1185)

CANCER, PATHOGENESIS, ETIOLOGY, TOBACCO (1597)
 CANCER, PRECURSOR ILLNESS (2264)
 CANCER, PREVALENCE RATES, BULLOUS DISEASE (1221)
 CANCER, SKIN CANCER, OCCUPATIONAL HAZARD (1277)
 CANCER CELLS, LYMPHOCYTE INTERACTIONS, HUMAN (2079)
 CANCER MORTALITY, NASAL CANCER, NICKEL PLANT WORKERS (2043)
 CANCER MORTALITY, SMOKING, TWIN PAIR (0109)
 CARCINOMA, INDUSTRIAL CARCINOGENS, PRIMATES, RODENTS, REVIEW (1747)
 CARCINOMA, METASTASIS PATTERN, YOSHIDA ASCITES SARCOMA (0322)
 CARCINOMA, TISSUE TYPE, URANIUM MINERS (1859)
 CARCINOMA OF THE BRONCHUS, PLASMA GROWTH HORMONE, HYPERTROPHIC OSTEOARTHROPATHY (0773)
 CELL, CIGARETTE SMOKE, GUINEA PIG (2261)
 CELLS, CARCINOMA, 3H-THYMIDINE, CHINESE HAMSTER (1675)
 CHANGES, RADIATION DAMAGE (1009)
 CHROMOSOMES, SV40, HAMSTER (1498)
 CURSCHMANN SPIRAL, CIGARETTE SMOKING (0104)
 DIETHYLNITROSAMINE, HAMSTER (2242)
 DIETHYLNITROSAMINE, LIVER, MICE (2245)
 DIMETHYLNITROSAMINE, MOUSE (2246)
 EARLY RADIOLOGICAL CHANGES, PULMONARY AND PLEURAL ASBESTOSIS (1263)*
 EMBRYONIC LUNG ORGAN, EXPLANT, MOUSE, GAS PHASE OF CIGARETTE SMOKE, CYTOCHEMISTRY (0501)
 EPITHELIOMA, MEDIASTINAL LYMPHOMA, URETHAN, VIRUS PARTICLES, GERM-FREE MOUSE (0494)
 FIBROBLASTS, SV40 (1490)
 GLASS FIBERS, OCCUPATIONAL HAZARD, CANCER REVIEW (0874)*
 GOAT, PULMONARY MUCOEPIDERMOID TUMOR (0301)*
 GRANULOMAS, ASBESTOS DUST, MICE, HAMSTERS (1852)
 HISTOCHEMISTRY, WHOLE BODY IRRADIATION, RAT (0127)
 HISTOLOGY, N-NITROSO-N-METHYLURETHANE, ALKALINE PHOSPHATASE, MOUSE (0486)
 HYPERPLASIA, FOCAL PROLIFERATION, TOBACCO, RABBIT (1833)
 INCIDENCE OF BRONCHOGENIC CANCER, AMERICAN NEGROES (1623)
 IRRADIATION, ADENOMA, TUMOR AGENT, MOUSE (2286)
 LIVER, CARCINOMA, HYDRAZINE SULFATE, MOUSE, ISONIAZIDE METABOLISM, MAN (0415)
 MESOTHELIOMA, ABDOMEN, ASBESTOS, FERRITIN, HUMAN (2257)
 MESOTHELIOMA, ASBESTOS EXPOSURE, ENGLAND (1858)
 MESOTHELIOMA, SILICOSIS, RADIATION (0996)
 MOUSE BRONCHIAL CELLS, MALIGNANT CHANGES, PARA-BENZOQUINONE INHALATION (1336)
 NEOPLASIA, OZONE, MICE (0884)
 NEOPLASMS, CHOLESTEROL, LIPID, DIET PITUITARY CHANGES (0397)
 NICKEL CARBONYL GAS (0510)
 NITROSOAZETIDINE, NITROSCHEPTA-METHENEIMINE, STOMACH (0086)
 OIL MIST EXPOSURE, RESPIRATORY TRACT CANCER (0276)
 OVINE PULMONARY ADENOMAS, ULTRASTRUCTURE OF TUMORS, VIRAL PARTICLES (1411)
 PATHOGENESIS, CANCER, TUBERCULOSIS (2472)
 PRIMARY CANCER, EPIDEMIOLOGY, ALESSANDRIA (1184)
 PULMONARY ADENOMATA, 3-METHYLCHOLANTHRENE, MICE (1806)
 PULMONARY CANCER, POLAND, INCIDENCE AND MORTALITY (1192)*
 PULMONARY CARCINOMA, MICE, CIGARETTE SMOKE (1367)
 PULMONARY FIBROSARCOMA, DIABETES MELLITUS (2145)*
 PULMONARY FUNCTION, ASBESTOS DUST, OCCUPATIONAL EXPOSURE (1857)
 PULMONARY ISCHEMIA, IONIZING IRRADIATION (0124)
 PULMONARY METASTASES, LYMPHANGIOSIS PATHOGENESIS, HUMAN (2473)
 PULMONARY TUMORS, HYDRAZINE SULFATE, OVARIAN HORMONE PRODUCTION (0910)
 RESPIRATORY FUNCTION, SPUTUM CYTOLOGY EXAMINATION, WOMEN CIGARETTE SMOKERS (0975)
 RETENTION IN ORGANS, BEAGLE DOGS, STRONTIUM 90 (1013)
 SCLEROTIC FOCI, PNEUMOCONIOSIS, NEOPLASTIC TRANSFORMATION (1153)
 SQUAMOUS EPITHELIAL CARCINOMA, STRUCTURAL CHANGES, BRONCHOGENIC (1662)
 SURFACE ACTIVITY, LECITHIN METABOLISM, EFFECTS OF RADIATION (0542)
 THORIUM 232, CIGARETTE SMOKERS (140)
 TOBACCO, EMPHYSEMA, SPONTANEOUS PNEUMOTHORAX, CANCER (1834)
 TRAUMA, CARCINOMA, PATHOGENESIS (1406)*
 TUMORS, 3,4-BENZOPYRENE, EFFECT OF SILICOTIC DUSTS, RAT (0122)*
 TUMORS, CYSTEINE S-CARBOXYL DERIVATIVE, NITROSAMINES (0083)
 TUMORS, INDUSTRIAL CARCINOGENS, REVIEW (1749)
 TUMORS, INDUSTRIAL CARCINOGENS, TUMOR MORPHOLOGY (1750)
 TUMORS, LIVER TUMORS, CYCASIN (0895)
 TUMORS, POLYVINYLPYRIDINE-N-OXIDE, INHALATION (1768)
 ULTRASTRUCTURE, WHOLE BODY IRRADIATION, RAT (0128)
 URETHAN, PHENOBARBITAL, MOUSE (0493)
 LYMPH
 NODE, SARCOMA, 3-METHYLCHOLANTHRENE, MOUSE (0471)
 NODE, URIDINE UPTAKE, DIMETHYLBENZ(

ANTHRACENE, ANTI-LYMPHOCYTE SERUM
 (0456)
 PH NODE
 CELLS, SV40, ANTIBODY (1097)
 IMMUNE, COLONY INHIBITION, RAT HEPA-
 TOMA (1550)
 LYMPHOSARCOMA, RETICULUM CELL SARCOMA
 (1236)
 REGIONAL, HOST RESPONSE TO TUMOR
 TRANSPLANT (1125)
 TUMOR IMMUNITY, MOUSE (2462)
 PHATICS
 MALIGNANT MELANOMA, MICROMETASTASES,
 PRIMARY TUMOR (0778)
 MOLONEY LEUKEMIA VIRUS VARIANT,
 TUMORIGENESIS IN MICE, VIRUS (1443)
 PHOBLAST
 ACUTE LEUKEMIA, KARYOTYPE STUDIES
 (1693)
 CYTOGENETICS, EPSTEIN-BARR VIRUS
 (1884)
 EPSTEIN-BARR VIRUS, INFECTIVITY AND
 CYTOPATHOLOGY (1023)
 HUMAN LYMPHOBLASTOID CELL LINES,
 EPSTEIN-BARR VIRUS (1435)
 LEUKEMIA, TRNA (1204)
 PHOCYTE
 AGGREGATE ENZYME, RNA SYNTHESIS,
 PHYTOHEMAGGLUTININ, HUMAN (1138)
 ANTILYMPHOCYTE SERUM, LEUKEMIA,
 MURINE VIRUS (1543)
 ANTILYMPHOCYTE SERUM, SARCOMA, MICE
 (2442)
 BENZENE, IRON METABOLISM, SINUS,
 FOLLICULAR (0983)
 BLASTOGENESIS, MUTAGENESIS, ADRIAMYCIN
 HUMAN (0699)
 BLASTOGENESIS, PROTEIN ACCUMULATION,
 PHYTOHEMAGGLUTININ STIMULATION
 (0697)
 CANCER PATIENTS, PHYTOHEMAGGLUTININ,
 TRANSFORMATION, ALLOGENEIC PLASMA
 (2460)
 CARCINOMA, SARCOMA, IMMUNITY, HUMAN
 (2418)
 CHROMOSOME, ABERRATION, RADIATION,
 HUMAN (1008)
 CYCLAMATE, CHROMOSOME ABERRATION (0418)
 DNA SYNTHESIS, LYMPHOGRANULOMA
 (2584)*
 HOST RESPONSE, CHILDREN, HODGKIN'S
 DISEASE (0756)
 INDUCTION, ANTIGEN, EPSTEIN-BARR
 VIRUS, MAN (2421)
 INFILTRATION, URINARY BLADDER
 CARCINOMA (1579)
 INTERACTIONS, HUMAN LUNG CANCER CELLS
 (2079)
 LYMPHOID CELLS, ALLOGRAFTS, ANTI-
 LYMPHOCYTE SERUM, MICE (1559)
 LYMPHOMA, MORPHOLOGICAL AND FUNCTIONAL
 CHANGES (1257)
 MIGRATION INHIBITING FACTOR, HEPATOMA,
 GUINEA PIG (2440)
 MIXED REACTION, AUTOCHTHONOUS STIMULA-
 TION, LEUKEMIA (1996)
 MONONUCLEAR CELLS, PHYTOHEMAGGLUTIN-
 IN-P, PERITONEAL FLUID (1572)

NORMAL AND NEOPLASTIC LYMPHOID CELL
 PROTEINS, ELECTROPHORETIC PATTERNS
 (1212)
 ORAL MUCOSA, LEUKOPLAKIA (1150)
 PHYTOHEMAGGLUTININ, FOLATE UPTAKE,
 HUMAN (0701)
 PHYTOHEMAGGLUTININ, IMMUNITY (1137)
 PHYTOHEMAGGLUTININ, SPLEEN, THYMUS
 (1122)
 PHYTOHEMAGGLUTININ CONSUMPTION,
 HODGKIN'S DISEASE (0733)
 PHYTOHEMAGGLUTININ-TRANSFORMED, MEGA-
 LOBLASTIC ANEMIA, MORPHOLOGY, DNA
 SYNTHESIS, HUMAN (0698)
 PRIMARY MELANOMA, METASTASIS (0722)
 PROLIFERATION, CONTROL, RECOGNITION
 SITE (0008)
 PROLIFERATION, IMMUNE RESPONSE,
 LYMPHOPROLIFERATIVE DISEASE, REVIEW
 (0391)*
 PROLIFERATION KINETICS, HODGKIN'S
 DISEASE, LYMPHADENOSIS, PHYTO-
 HEMAGGLUTININ (1720)*
 PUROMYCIN, ACTINOMYCIN D, PHYTO-
 HEMAGGLUTININ (1678)
 RESPONSE, HUMAN, AUTOCHTHONOUS TUMOR
 CELLS (1574)
 RESPONSE, PHYTOHEMAGGLUTININ, DOWN'S
 SYNDROME (1570)
 SENSITIZATION, BASIC PROTEIN ANTIGENS,
 CANCER TEST (1197)
 SPLEEN, TRANSPLANT, RAT (2429)
 THYMIC, SPLEEN, LACTIC DEHYDROGENASE
 PASSENGER VIRUS, RAUSCHER LEUKEMIA
 VIRUS (0609)
 THYMIC, X-IRRADIATION, NUCLEOLAR
 MORPHOLOGY (1842)
 THYMUS, MICE, IMMUNOLOGY (0842)
 TRANSFORMATION, CYCLIC AMP, PHYTO-
 HEMAGGLUTININ (0236), (0702)
 TRANSFORMATION, DNA SYNTHESIS, ALPHA-
 AMINO-P-TOLUENESULFONAMIDE, HUMAN
 (0508)
 TRANSFORMATION, LYMPHOMAS, PHYTO-
 HEMAGGLUTININ, CELL CULTURE (0239)
 TRANSFORMATION, PHYTOHEMAGGLUTININ,
 CANCER PATIENTS (1998)
 TRANSFORMATION, PHYTOHEMAGGLUTININ,
 DNA POLYMERASE, REPLICATION (0703)
 TRANSPLANTED CARCINOMA, LYMPHOID CELL
 REACTION (2408)
 TRANSPLANTED CARCINOMA, REACTION
 (2433)
 LYMPHOCYTOSIS
 BOVINE LEUKOSIS, COINCIDENCE IN CATTLE
 HERDS (2128)
 LYMPHOGRANULOMATOSIS
 EPIDEMIOLOGY, CHILDREN, BULGARIA
 (2483)
 EPIDEMIOLOGY, POLAND (1629)*
 LYMPHOMA
 ANTIGENIC STIMULATION, IMMUNO-
 SUPPRESSIVE TREATMENT (1539)
 BURKITT'S, MALARIA, AFRICA (0006)
 CELLULAR AND HUMORAL IMMUNE RESPONSE,
 GROSS VIRUS (1531)
 CYTOTOXIC ANTIBODY RESPONSE, GROSS
 LEUKEMIA VIRUS (1520)

DIFFERENTIAL GEOGRAPHIC PREVALENCE,
 MULTIPLE MYELOMAS (0267)
 DOUBLE-STRAND DNA BREAKS, X-IRRADIATION,
 MURINE (0523)
 ENDOPLASMIC RETICULUM, GOLGI COMPLEX,
 IMMUNOGLOBULIN (2009)
 EPSTEIN-BARR VIRUS, INFECTIOUS MONONUCLEOSIS,
 HUMANS (0875)*
 FELINE, C-TYPE VIRUS PARTICLES, ENVELOPE SPIKES
 (0588)
 GROSS VIRUS, ANTITHYMOCYTE SERUM (1035)
 HAMSTER PAPILLOMAS, PAPOVA VIRUS (1956)
 HERPES SAIMIRI, MARMOSET (2341)
 HERPESVIRUS SAIMIRI, ACUTE LYMPHOCYTIC
 LEUKEMIA (1464)
 HUMAN, HOUSEHOLD QUESTIONNAIRE SURVEY,
 DOMESTIC CATS (1182)
 HUMAN CELLS, INDUCTION OF LEUKEMIA IN
 MICE, LATENCY (2136)
 IMMUNOGLOBULINS, MICE (2441)
 IMMUNOLOGICAL FACTOR (0354)
 INACTIVATION, IRRADIATION, IMMUNOLOGY,
 MOUSE (0223)
 L1210, DIHYDROFOLATE REDUCTASE (1646)
 LANDSCHUTZ, KARYOTYPE (2524)
 LEUKEMIA, AUTOIMMUNE RESPONSE (0009)
 LEUKEMIA, PHENYLALANINE TRANSFER RNA,
 HUMAN (2520)
 MALIGNANT, HERPESVIRUS SAIMIRI, MONKEYS
 (1917)
 MALIGNANT, LYMPHOCYTES, ANTIGENS (1542)
 MALIGNANT, METHYLNITROSOUREA, DOSE AND
 SCHEDULE EFFECT, MICE (0088)
 MALIGNANT LYMPHOPROLIFERATIVE DISEASE,
 ACID PHOSPHATASE ACTIVITY, NONSPECIFIC
 ESTERASE ACTIVITY (0257)
 MANDIBULAR, 7,12-DIMETHYLBENZ(A)-ANTHRACENE,
 TOOTH SOCKET (1788)
 MEDIASTINUM, URETHAN, PARTICLES, VIRUS
 (0495)
 MICE, SPLEEN CELL (0224)
 MOLONEY LEUKEMOGENIC VIRUS, PLASMODIUM
 BERGHEI YOELII (0600)
 MORPHOLOGICAL AND FUNCTIONAL CHANGES,
 LYMPHOCYTES IN CULTURE (1257)
 MORPHOLOGY, BURKITT TUMOR, EPSTEIN-BARR
 VIRUS (0575)
 MURINE, MACROPHAGE, IMMUNE LYMPHOID
 CELLS (0725)
 MURINE, MOLONEY LEUKEMIA VIRUS (1077)
 MYELOMA HYBRID, ANTIGEN, PROTEIN SYNTHESIS
 (1124)
 ORGAN TRANSPLANTS, IMMUNOSUPPRESSION,
 ANTIGEN, HYPERPLASIA (1589)
 PHYTOHEMAGGLUTININ, DNA SYNTHESIS, MURINE
 (1997)
 REOVIRUS 3, MURINE (2316)
 ROWSON-PARR VIRUS, MICE (0610)
 THYMUS, LEUKEMOGENIC ACTIVITY, 7,12-DIMETHYLBENZ(A)
 ANTHRACENE (1896)
 LYMPHOMYELOMA
 RADIUM POISONING, OSTEOSARCOMA (0001)

LYMPHOPROLIFERATIVE DISEASE
 ATYPICAL DYSGLOBULINEMIA, CHROMOSOMAL ANOMALIES
 (0343)*
 IMMUNE RESPONSE, LYMPHOCYTE PROLIFERATION,
 REVIEW (0391)*
 LYMPHOID MALIGNANCIES, IMMUNE DEFICIENCY,
 PREDISPOSITION (1723)
 PATHOGENESIS, IMMUNOLOGICAL DISORDER REVIEW
 (1760)*
 WALDENSTROM'S MACROGLOBULINEMIA, ABNORMALLY
 LARGE CHROMOSOME, COLCHICINE (1688)
 LYMPHOSARCOMA
 ACUTE LYMPHOBLASTIC LEUKEMIA, LYMPHOID
 CELL PROLIFERATION IN VITRO, ESTRADIOL-17
 BETA, MAN (0342)*
 AFFECTED SIBLINGS, CYTOGENIC ABNORMALITY
 (0694)
 BOVINE, VIRUS IN BOVINE CELLS (1873)
 BURKITT'S LYMPHOMA, MALARIA (0689)*
 CATTLE, BOVINE SYNCYTIAL VIRUS, MORPHOLOGICAL
 VARIANT (0563)
 CYTOPATHIC EFFECT, MIXED CELL CULTURES,
 VIRUS, BOVINE (1876)
 EHRlich'S CARCINOMA, PROTEIN-BOUND CALCIUM
 (1233)
 EPSTEIN-BARR VIRUS, JUVENILE BURKITT LYMPHOMA,
 NECK, GERMANY (0152)
 IMMUNOCYTE CLONAL EVOLUTION, AUTOIMMUNE
 DISEASE (0719)
 LEUKEMIA VIRUS PARTICLES, MORPHOLOGY AND
 DISTRIBUTION, VIRUS (0550)
 LYMPH NODE, RETICULUM CELL SARCOMA (1236)
 LYMPHOCYTES, SPLEEN, BOVINE (2036)
 NEWBORN AND WEANED MICE, N-NITROSOMETHYLUREA
 (0962)
 RABBIT, GENETICS AND PATHOLOGY (0802)
 SKIN GRAFTS, MICE (1558)
 THYMUS, PIKE (2126)
 THYMUS-INDEPENDENT, PREDNISOLONE, MURINE
 LYMPHOMA VIRUS (0167)
 TOAD, COCKROACH VECTOR (0565)
 TRANSMISSION OF DISEASE, FELINE, EPIDEMIOLOGY
 (2044)
 TRANSMISSION OF DISEASE, VIRUS PARTICLES,
 BOVINE (2129)
 TRANSPLANTATION OF TUMORS, IMMUNOSUPPRESSION,
 BOVINE (2012)
 TRANSPLANTATION PASSAGE IN DOGS, GUINEA PIG,
 CANINE (2132)
 LYSINE
 5-N-METHYLATED, ERLICH SUBCUTANEOUS CARCINOMA,
 GROWTH-PROMOTING EFFECTS (0816)
 LYSOPINE
 OCTOPINE, PLANT TUMORIGENESIS PROMOTERS
 (0404)
 MACROPHAGE
 ALVEOLAR, BENZO(A)PYRENE, RATS, LUNG (0936)
 ALVEOLAR CELL CARCINOMA, DNA CONTENT (0736)
 COLONY FORMING CELLS, TUMOR, MICE (2404)
 IMMUNE LYMPHOID CELLS, MURINE LYMPHOMA
 (0725)

INHIBITION OF MIGRATION, TUMOR ANTIGEN (1554)
MIGRATION, DELAYED HYPERSENSITIVITY REACTION, TUMOR IMPLANT (0228)
MIGRATION, FRIEND LEUKEMIA VIRUS, IMMUNITY (1534)
RIA
BURKITT'S LYMPHOMA, AFRICA (0006)
BURKITT'S LYMPHOMA, EPSTEIN-BARR VIRUS, AUTOIMMUNE SYSTEM (0005)
BURKITT'S LYMPHOMA, LYMPHOSARCOMA (0689)*
COCARCINOGEN, BURKITT'S LYMPHOMA (0690)*
GNANT MELANOMA INDUCTION
URETHAN (0497)
GINOMA
RADIATION, THERAPEUTIC DOSE (0370)
ARY GLAND
ADENOCARCINOMA, 7,12-DIMETHYLBENZ-ANTHRACENE, ESTROGEN INTERACTION, RAT (0064)
ADENOCARCINOMA, GLUCOSE METABOLISM, ACETATE, MOUSE (2553)
ADENOCARCINOMA, IMMUNOSUPPRESSIVE THERAPY (0695)
ADENOCARCINOMA, NUCLEIC ACID ESTIMATION, BASIC PROTEIN ESTIMATION (0190)
ADENOCARCINOMA, TESTOSTERONE, ESTROGEN (0448)
ADENOCARCINOMA, THYMIC LYMPHOSARCOMA, 4(5)-(3,3-DIMETHYL-1-TRIAZENO)IMIDAZOLE-5(4)-CARBOXAMIDE (0423)
BENIGN, MALIGNANT, FIBROSA CYSTICA, FIBROMATOSIS, FIBROADENOMA (029)
BILATERAL CANCER, INCIDENCE, PATHOLOGY (1266)*
BITTNER VIRUS, LEUKEMIA, GROSS VIRUS, MOUSE (1928)
BREAST CANCER, CALCIUM DEPOSITS, X-RAY, FAT TRANSPLANTATION (1010)
BREAST CANCER INCIDENCE, WHITE-NEGRO GENETIC ADMIXTURE (1699)
BREAST CANCER MORTALITY, REGIONAL VARIATIONS IN ENGLAND, DAIRY PRODUCT CONSUMPTION (2047)
BREAST CANCER RISK, AGE AT FIRST BIRTH, GLOBAL EPIDEMIOLOGICAL STUDY (1187)
CANCER, ANTIBODIES, MURINE MAMMARY TUMOR VIRUS (1929)
CANCER, EPIDEMIOLOGY, HUMAN, CANINE (0277)
CANCER, EPIDEMIOLOGY, QUEBEC (0298)*
CANCER, LACTATION, PREGNANCY (0321)
CANCER, 6-METHYLTHIOURACIL, HYPOTHYROIDISM, HYPERESTRINISM, RAT (0886)
CANCER, MORBIDITY RATES IN HUNGARY (0294)*
CANCER, SS PHENOTYPE, S BLOOD-ANTIGENS (1130)
CANCER, SUGAR AND FAT INTAKE, BLOOD GROUP A (0265)
CARCINOGENESIS, ESTROGEN TREATMENT, X-IRRADIATION (1295)
CARCINOGENESIS INHIBITION, PROLACTIN (0440)

CARCINOMA, ACIDIC NUCLEAR PROTEINS, ENZYME ACTIVITY (0338)*
CARCINOMA, ANDROGEN SECRETION, ENDOCRINE IMBALANCE (1751)*
CARCINOMA, COLLAGENASE, DNA, NITROGEN, INVASION (1649)
CARCINOMA, DIMETHYLBENZ(A)ANTHRACENE, ESTROUS CYCLE, RAT (1794)
CARCINOMA, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, IMMUNOLOGY, RAT (0454)
CARCINOMA, ETIOLOGY, PATHOGENESIS, REVIEW (1757)*
CARCINOMA, HUMAN, VIRUS, TUMOR-SPECIFIC NEOANTIGEN (1131)
CARCINOMA, IMMUNITY, RADIATION, MICE (2416)
CARCINOMA, LEUKOCYTES, VIRUS, LUNG (1420)
CARCINOMA, MAMMARY TUMOR VIRUS (0633)
CARCINOMA, 3-METHYLCHOLANTHRENE, KARYOTYPE, MOUSE (1340)
CARCINOMA, ORAL CONTRACEPTIVES (0984)
CARCINOMA, OTHER BREAST, REVIEW (0014)
CARCINOMA, RAT, DIMETHYLBENZ(A)-ANTHRACENE, INSULIN (0450)
CARCINOMA, RAT, 9,10-DIMETHYL-1,2-BENZANTHRACENE (0442)
CARCINOMA, RNA-TYPE VIRUSES, MONKEY (0626)
CARCINOMA, THYROID, SIPPLE'S SYNDROME (2581)*
CARCINOMA, TUMOR-SPECIFIC ANTIGEN, RAT (1132)
CARCINOMA, WEIGHT, AGE AT FIRST PREGNANCY (1618)
CARCINOMA, WOMEN, SURVIVAL RATE (0287)
CARCINOMA GROWTH, 2-BR-ALPHA-ERGO-CRYPTINE, ENDOCRINE FUNCTION (0930)
CERVIX, SKIN, IRAN, EPIDEMIOLOGY (0284)
COMEDOCARCINOMA, HISTOLOGICAL EXAMINATION, ORAL CONTRACEPTIVE (0505)
7,12-DIMETHYLBENZ(A)ANTHRACENE
HORMONAL ANTITUMOR AGENTS, RAT (0457)
NUCLEAR RNA POLYMERASE ACTIVITY, RAT (1791)
TESTOSTERONE, OVARIETOMY, MOUSE (1145)
DOUBLE MALIGNANCY, UTERUS (0299)*
EPITHELIAL CELLS, ENZYME ACTIVITY, ESTROGEN, RAT (2470)
EPITHELIOMA, CHRONIC CYSTIC MASTITIS, MALIGNANT TRANSFORMATION (1159)
FATTY TISSUE, SURFACE MOTILITY, CELLS (1679)
FEMALE REPRODUCTIVE ORGANS, MULTIPLE PRIMARY TUMORS (1621)
FIBROADENOMA, ADOLESCENTS (1705)
FIBROADENOMA, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, LACTOSE, RAT (2223)
HYPERPLASTIC ALVEOLAR NODULE, PHENYLALANINE, MOUSE (2191)
HYPERPLASTIC NODULE, ERGOCORNINE, 2-BR-ALPHA-ERGOKRYPTIN, MICE (0312)
HYPERPLASTIC NODULE, ERGOCORNINE, 2-BROMO-ALPHA-ERGOKRYPTIN (1207)

HYPOTHALAMUS, TUMOR, MOUSE (2501)
 KIDNEY, TUMORS, MOUSE (0811)
 MILK, MAMMARY TUMOR VIRUS (1067)
 MULTIPLE FIBROADENOMAS, HORMONAL
 CONTRACEPTIVES (1378)*
 MULTIPLE TUMORS, CERVIX, THERAPY,
 INCIDENCE (2137)
 NEOPLASIA, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, ISOENZYMES, OOPHORECTOMY
 RAT (2222)
 NEOPLASIA, IRRADIATED GRAFT,
 X-IRRADIATION (1847)
 NODULE OUTGROWTH LINE D BALB/C,
 MAMMARY TUMOR VIRUS, METHYLCHOL-
 ANTHRENE (0076)
 NUCLEAR RNA, NEOPLASTIC DEVELOPMENT,
 MURINE (2062)
 PROLACTIN, MITOTIC ACTIVITY, RAT
 (1676)
 SPINDLE CELL BREAST SARCOMA,
 RHABDOMYOSARCOMATOUS INCLUSIONS,
 METAPLASTIC INCLUSIONS (1264)*
 SPONTANEOUS, ADENOCARCINOMA, VIRUS
 PARTICLES (0630)
 SPONTANEOUS CARCINOMA, RUDIMENTS, RAT
 (2127)
 STRAIN DIFFERENCES, HORMONE, LOBULOAL-
 VEOLAR DIFFERENTIATION, MOUSE
 (0769)
 TAIWAN, CANCER, EPIDEMIOLOGY (2491)
 TRANSPLANT HISTOGENESIS, ISOGRAFT
 (1665)
 TUMOR, ANTISERA, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, RAT (1990)
 TUMOR, ASPIRATION BIOPSY, CYTOLOGIC
 DIAGNOSIS (0262)*
 TUMOR, CELL POPULATION KINETICS,
 CAPILLARY ENDOTHELIAL CELLS (0762)
 TUMOR, FRIEND LEUKEMIA VIRUS,
 RADIATION, MOUSE (2348)
 TUMOR, HORMONE-DEPENDENT, MURINE (2112)
 TUMOR, HORMONE RESPONSIVENESS,
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 (0060)
 TUMOR, HORMONES, STIMULATION OF
 TUMORIGENESIS (1215)
 TUMOR, HYPOTHALAMIC LESION, PROLACTIN
 (0770)
 TUMOR, KLINEFELTER'S SYNDROME, MAN
 (2566)
 TUMOR, LEUKEMIA, B PARTICLES,
 C PARTICLES, MOUSE (2410)
 TUMOR, LEUKEMIA, C-TYPE VIRUS
 PARTICLES, RAT (1870)
 TUMOR, MAST CELLS, 7,12-DIMETHYL(A)-
 ANTHRACENE, RAT (2227)
 TUMOR, 3-METHYLCHOLANTHRENE, DNA
 (1802)
 TUMOR, MURINE TRACE ANTIGEN (2422)
 TUMOR, N-NITROSOBUTYLUREA, LEUKEMIA,
 MICE, RATS (0092)
 TUMOR, NUCLEIC ACIDS (2081)
 TUMOR, PHOSPHATASE ENZYMES, ENZYME
 DISTRIBUTION, MOUSE (1144)
 TUMOR, PREGNANCY, 5-HYDROXYTRYPTAMINE
 (1226)
 TUMOR, PROLACTIN, 7,12-DIMETHYLBENZ-
 (A)ANTHRACENE (0927)

TUMOR, RESERPINE, 7,12-DIMETHYLBENZ
 (A)ANTHRACENE (0929)
 TUMOR, SPLENECTOMY, THYMECTOMY (062)
 TUMOR, SPLENECTOMY, THYMECTOMY,
 URETHAN (0099)
 TUMOR, VIRUS, ANTIBODIES, MICE (245)
 TUMOR, VIRUS, ANTIGEN, MURINE (2160)
 TUMOR, VIRUS PARTICLE, ELECTRON
 MICROSCOPIC STUDY (0146)
 TUMOR, VIRUS PARTICLES, HEMATOPOIET
 ORGANS, THYMUS, EPIDIDYMIS, MOUSE
 (0632)
 TUMOR CELLS, PROTEIN SYNTHESIS,
 LABELED METHIONINE INCORPORATION,
 MOUSE (0793)
 TUMOR ENHANCEMENT, 7,12-DIMETHYLBENZ
 (A)ANTHRACENE, BACILLUS CALMETTE-
 GUERIN (1243)
 TUMOR INCIDENCE, MAMMARY TUMOR VIRUS
 MOUSE INBRED STRAINS (1471)
 TUMOR SUPPRESSION, 7,12-DIMETHYLBENZ
 (A)ANTHRACENE, ACTINOMYCIN D (093)
 TUMOR VIRUS, AMINOPEPTIDASE ACTIVIT
 (1470)
 TUMOR VIRUS, CELL FUSION, MURINE
 (1926)
 TUMOR VIRUS, FOSTER-NURSING, TRANS-
 MISSION (0193)
 TUMOR VIRUS, HUMAN MILK (1419)
 BYPASS, 7,12-DIMETHYLBENZ(A)ANTHR
 CENE (1792)
 TUMOR VIRUS, RNA, ANTIGEN CROSS-
 REACTION (1927)
 TUMORIGENESIS, THYMECTOMY, INFLUENC
 OF MOUSE STRAIN (0192)
 VIRUS, IMMUNOGENICITY, MICE (2402)
 MAREK'S DISEASE
 CHICKEN EMBRYO, AGENT (1915)
 CYTOPATHIC EFFECT, HERPES TYPE VIRU
 VIRUS (1030)
 HERPES-TYPE VIRUS (1031)
 HERPES-TYPE VIRUS, VIRUS PROPAGATIO
 IN CULTURE (1029)
 HERPESVIRUS, IMMUNE RESPONSE IN
 CHICKENS (1468)
 HERPESVIRUS, INFECTIVITY, ANTIGEN (0
 PERIPHERAL NERVE LESIONS, RETICULO-
 ENDOTHELIOSES VIRUS (0161)
 SCIATIC NERVE LESION (0158)
 SENDAI VIRUS (0581)
 VIRUS, HERPESVIRUS, BURSECTOMY (016
 VIRUS, HERPESVIRUS CAL-1, PLAQUE
 TYPE, TISSUE CULTURE (0159)
 MAST CELLS
 CROTON OIL, INFLAMMATION, RAT (2182)
 MASTOCYTOMA
 CANINE, MUCOSUBSTANCES (0329)
 CELLS, CYTOTOXIC REACTION, PHOSPHO-
 LIPID METABOLISM (2057)
 MEDIASTINUM
 LYMPHOMA, LUNG EPITHELIOMA, URETHAN
 VIRUS PARTICLES, GERM-FREE MOUSE
 (0494)
 LYMPHOMA, URETHAN INDUCED, VIRUS-LI
 PARTICLES (0495)
 MEIOSIS
 ABNORMALITIES, URETHAN, ETHYL
 METHANESULFONATE (1828)

WIN
 CARCINOGENESIS, REVIEW (1283)*
 KERATINOCYTES, BASAL CELL CARCINOMA
 (2106)
 SYNTHESIS, PROLIFERATION, MOUSE
 PIGMENT CELL (0812)
 NOMA
 ACUTE LEUKEMIA, ANTIGENICITY IN HUMAN
 TUMORS (1129)
 AMINO ACIDS, MITOCHONDRIA, LIVER,
 HAMSTER (2540)
 B16, SPONTANEOUS, METASTASIS, MOUSE
 (0078)
 CARCINOMA, 8-GLUCURONIDASE, PHENOL-
 PHTHALEIN, MOUSE (2085)
 DIMETHYLBENZANTHRACENE, SKIN,
 HAMSTER (0118)*
 EXPOSURE TO SUNLIGHT (0835)
 FISH, XIPHOPHORUS, CROSS BREEDING,
 SEX (2522)
 GROWTH, XIPHOPHORIN FISH, ALBINO
 (2559)
 HARDING-PASSEY, ULTRASTRUCTURE, MURINE
 (2543)
 HUMAN, CHANGES DURING MITOSIS, GOLGI
 APPARATUS (0786)
 INCIDENCE IN UTAH, SURVIVAL RATE
 (1614)
 LYMPHATICS, MALIGNANT, MICROMETASTASES
 PRIMARY TUMOR (0778)
 LYSOSOMAL ENZYME, MOUSE (2542)
 LYSOSOMAL ENZYME ACTIVITY, TUMOR
 GROWTH, MOUSE (1248)
 MALIGNANT, CELTIC POPULATION, GENETIC
 PREDISPOSITION (2093)
 MALIGNANT, CONJUNCTIVA (0749)
 MALIGNANT, DIAGNOSIS, EPIDEMIOLOGY
 (1632)*
 MALIGNANT, MELANOCYTE, ULTRASTRUCTURE
 (2560)
 MELANOCYTOMA, NEVOCYTOMA, REVIEW
 (0846)
 OCULAR, ULTRASTRUCTURE, SURFACE
 PROPERTIES (1670)
 PRIMARY, METASTATIC, LYMPHOCYTIC
 REACTION (0722)
 RADIATION THERAPY, FACE AND LIP
 (0547)
 RNA, HARDING-PASSEY CELLS, LIVER,
 MUSCLE, RAT (2077)
 SARCOMAS, IMMUNOCOMPETENCE, IMMUNO-
 THERAPY, HUMAN (0704)
 SKIN GENETICS, MAN (0830)*
 TUMOR EMBOLI, METASTASIS, DISTRIBUTION
 OF LABELED TUMORS (0822)
 TUMOR EXTRACT, LYMPHOCYTE STIMULATION,
 IMMUNOLOGY (0230)
 TUMOR-SPECIFIC IMMUNITY, HUMAN (2438)
 TYROSINASE, PROPERTIES, MURINE (2541)
 HALAN
 MULTIPLE MYELOMA, ACUTE MYELOMONOCYTIC
 LEUKEMIA (0507)
 URANE
 AGGLUTINATION, POLYOMA VIRUS, NON-
 TRANSFORMING MUTANT (0680)
 BLOOD LYMPHOCYTE CELL, ULTRASTRUCTURE
 OF ACID CARBOHYDRATES, HUMAN
 LYMPHOID LEUKEMIA (2142)*

CELL SURFACE GLYCOPROTEINS, VIRUS,
 GROWTH PHASE (1939)
 CELLULAR TRANSMEMBRANE ELECTRICAL
 POTENTIAL, MITOSIS, MALIGNANT CELLS
 (1677)
 CHICK CHORIOALLANTOIC, ROUS SARCOMA
 VIRUS, URIDINE METABOLISM (0643)
 GLYCOPEPTIDES, VIRUS-TRANSFORMED
 CELLS, POLYOMA (1957)
 INFECTED CELL, MUCOPOLYSACCHARIDE
 LAYER, FUJINAMI ROUS SARCOMA VIRUS
 (1948)
 MALIGNANT CELL, CELL SURFACE ELECTRIC
 POTENTIAL (0252)
 MICROSOME, LIVER, NUCLEIC ACID,
 CHEMICAL CARCINOGEN, RAT (0913)
 PHOSPHOLIPIDS, HEPATOMA CELLS,
 CALCIUM, MAGNESIUM (1651)
 PLASMA, LIVER CELLS, HEPATOMA, ATPASE
 ACTIVITY (0258)
 PROTEINS, MITOCHONDRIA, LIVER,
 HEPATOMA, RAT (1652)
 SMOOTH, ROUGH, MYELOMA, MOUSE (1667)
 TRANSFORMED CELL, SURFACE, CARBO-
 HYDRATE LOCATION (0708)
 TUMOR CELL, SIALIC ACID TRANSFERASE
 (1101)
 MENINGIOMA
 BENIGN, RING CHROMOSOME, HUMAN (2092)
 CHROMOSOME, HUMAN (2519)
 HYPERDIPLOIDY, CHROMOSOMES, HUMAN
 (1692)
 INTRACRANIAL, FAMILIAL, SURGERY (1262)
 MENINGOTHELIAL, GLYCOGEN GRANULES,
 HUMAN (2104)
 PHILADELPHIA CHROMOSOME, HUMAN (2532)
 MESENCHYMAL TUMORS
 DIMETHYLNITROSAMINE, KIDNEY, RAT
 (0950)
 SPONTANEOUS, NEWT (2555)
 MESOTHELIOMA
 ABDOMINAL CARCINOMA, ACTINOMYCIN D (0024)
 ASBESTOS, OCCUPATIONAL EXPOSURE,
 EPIDEMIOLOGY (2481)
 ASBESTOS EXPOSURE (0268)
 ASBESTOS EXPOSURE, NETHERLANDS
 SHIPYARDS (2046)
 DIFFUSE PLEURAL, ASBESTOS EXPOSURE,
 CLINICAL FEATURES (1004)
 PLEURAL, ENGLAND, ASBESTOS EXPOSURE
 (1858)
 SCOTLAND, OCCUPATIONAL EXPOSURE TO
 ASBESTOS (1170)
 METABOLISM
 ABERRATION, ENDOCRINE DISEASES,
 MALIGNANCIES (0011)
 N-ACETYLATION, NORMAL AND NEOPLASTIC
 RAT LIVER, HEPATOMA HISTONE (2056)
 ADENINE NUCLEOTIDE, ASCITES TUMOR
 CELLS, MICE (2065)
 BENZO(A)PYRENE, PRETREATMENT, INDUC-
 TION, RAT BILE (1334)
 CANCER PATIENTS, HORMONAL ABNORMAL-
 ITIES, DISCRIMINANT FUNCTION (0372)
 CARBOHYDRATES, ADENOVIRUS TYPE-12, RAT
 (2333)
 CATECHOLAMINE, NEOPLASTIC TISSUE, MAN
 (2587)*

- CHANGES, THIOACETAMIDE, LIVER TUMORS (0970)
- CHOLESTEROL, MORRIS HEPATOMA (2548)
- DIBENZ(A,H)ANTHRACENE, EPOXIDE INTER-MEDIATE, LIVER, RAT (2221)
- DIMETHYLNITROSAMINE, AMINOACETONITRILE (0961)
- EHRlich ASCITES CARCINOMA, SARCOMA 180, ESSENTIAL FATTY ACIDS, WHOLE BLOOD (1655)
- ELIMINATION, 4-NITROQUINOLINE-1-OXIDE, RAT (0967)
- ENERGY EXPENDITURE, WALKER TUMOR, RAT (1703)
- GLIOBLASTOMA, LACTATE PRODUCTION, TUMOR REGIONAL HISTOCHEMISTRY, MOUSE (1698)
- GLUCOSE, ACETATE, MAMMARY ADENOCARCINOMA, MOUSE (2553)
- GLUCOSE, CANCER BIOCHEMISTRY, REVIEW (0007)
- GLUCOSE, LEUKEMIA AND DIABETES, DNA SYNTHESIS (0775)
- GLUCOSE, RADIATION, MOUSE (2284)
- GLUCOSE INCORPORATION, NOVIKOFF ASCITES HEPATOMA CELLS, CYTOPLASMIC GLYCOGEN FOCI (2061)
- GLYCOGEN, GLYCOGEN SYNTHETASE, HEPATOMAS, RAT (2086)
- GLYCOGENESIS, HEPATOMA, ULTRASTRUCTURE (2073)
- GLYCOLYSIS, RAT EMBRYO FIBROBLASTS, ADENOVIRUS TYPE 12, 6, 3, HAMSTER SARCOMA (1048)
- HYDROGEN TRANSPORT, LEUKEMIA, BONE MARROW (2060)
- LIPID, SKIN, LIGHT, RADIATION (1856)
- MALIGNANT NEOPLASMS, LIVER, OLEIC ACID, LINOLEIC ACID, STEARIC ACID (1639)
- METHYL METHANESULFONATE, ETHYL METHANESULFONATE, MOUSE (0902)
- NOVIKOFF HEPATOMA, GLUCOSE, ADENINE NUCLEOTIDES, ENERGY (2539)
- NUCLEIC ACID, PROLIFERATING COLONIC CELLS, NEOPLASTIC LESIONS (2076)
- PHOSPHOLIPID, MASTOCYTOMA CELLS, CYTOTOXIC REACTION (2057)
- PROTEIN, MAMMARY GLAND TUMOR, METHIONINE INCORPORATION, MOUSE (0793)
- PROTEOLIPID, WALKER RAT SARCOMA (2068)
- PYRUVATE, X-IRRADIATION, THYMOCYTES, RAT (2293)
- SPERMIDINE AND PUTRESCINE SYNTHESIS, POLYAMINE ACCUMULATION, MURINE LEUKEMIA L1210 (2074)
- 32 PHOSPHORUS INCORPORATION, MAMMARY TUMOR TISSUE (2081)
- 35 SULFUR UPTAKE, COLONIC MUCOSA, CARCINOMA (2069)
- URIDINE, CHICK CHORIOALLANTOIC MEMBRANE, ROUS SARCOMA VIRUS (0643)
- METAL
- CARCINOGENIC METAL CHELATES, FOLIC ACID (1292)
- COBALT CHLORIDE, SODIUM COBALTNITRIDE, PROMOTION OF TUMOR GROWTH (1339)
- HEAVY IONS, CARCINOGENICITY, DIMETHYL SULFOXIDE, HYDROGEN PEROXIDE (218)
- HUMAN TISSUES, BENIGN, MALIGNANT, MICROPROBE ANALYSIS (2134)
- MAGNESIUM CHLORIDE, ENHANCED PLAQUE FORMATION, VIRUS, ADENOVIRUS (105)
- NICKEL, REVIEW (2154)
- METAPLASIA
- INTESTINE, EPIDEMIOLOGY, JAPAN (248)
- LUNG CANCER, MICE, INFLUENZA VIRUS (0564)
- TRACHEAL EPITHELIUM, MORPHOLOGY, VITAMIN A DEFICIENCY, RAT (1209)
- METASTASIS
- DISTRIBUTION OF LABELED TUMORS, MELANOMA TUMOR EMBOLI (0822)
- EHRlich ASCITES CARCINOMA, GROWTH IN CHICK EMBRYO (2144)*
- HAMSTER TUMORS, LYSOSOMAL CHANGES, LIVER, NONIONIC SURFACTANTS (1680)
- IMMUNE STATUS, FIBROSARCOMA, MICE (2425)
- MALIGNANT TROPHOBLASTIC TERATOMA, TESTICULAR TUMORS (2116)
- MELANOMA, PRIMARY MELANOMA, LYMPHOCYTIC REACTION (0722)
- 20-METHYLCHOLANTHRENE, MELANOMA B16 SARCOMA (0078)
- MICROMETASTASES, LYMPHATICS, MELANOMA PRIMARY TUMOR (0778)
- MIGRATION OF TUMOR CELLS, INVASION, CHEMOTACTIC CANCER CELL FACTOR (1682)
- MURINE PLASMACYTOMA, BONE LESIONS (2143)*
- NEOPLASMS, BLOODBORNE, MODEL (1681)
- OVARIAN CARCINOMA, ACUTE MYELOGENOUS LEUKEMIA, CYTOSTATIC TREATMENT (0506)
- PATTERN, ADENOCARCINOMA, THYROID, HUMAN (0823)
- PRIMARY TUMOR, DNA, HUMAN (2516)
- ROUS SARCOMA, VIRUS, CHROMOSOME, RAT (1084)
- SARCOMA, IMMUNIZATION, RAT, 7,12-DIMETHYLBENZ(A)ANTHRACENE (0455)
- SPREAD OF INOCULATED TUMOR CELLS, WALKER 256 TUMOR, ULTRASTRUCTURE (1683)
- WALKER'S CARCINOMA, GASTRIC WALL, RAT (0763)
- YOSHIDA ASCITES SARCOMA, LUNG CARCINOMA (0322)
- METHANESULPHONOXY-ALKANE
- METHYL METHANESULPHONATE, ETHYL METHANESULPHONATE, ISOPROPYL METHANESULPHONATE, BLOOD, SPLEEN COLONY (0413)
- METHIONINE SULFOXIMINE
- X-IRRADIATION, BONE MARROW CELL CULTURE (0405)
- METHOTREXATE
- HEPATOMA, LUNG ADENOMA, CARCINOMA, MOUSE (2185)
- ROUS SARCOMA VIRUS, L-ASPARAGINASE, INHIBITION OF FOCUS-FORMATION (1480)

-METHOXY-4-AMINOAZOBENZENE
 HEPATOMA, TARGET ORGANS, DOSE EFFECT
 (0055)
 ETHYL METHANE SULFONATE
 METABOLISM, MOUSE (0902)
 UNSCHEDULED DNA SYNTHESIS, MUSCLE, RAT
 (2201)
 ETHYLATION
 EMBRYONIC TISSUE, ONCOGENIC SYSTEMS,
 TRNA, LEUKEMIA (2503)
 GUANOSINE, CYTOSINE, IMMUNITY, TRNA
 (2089)
 5-METHYLURIDINE, TRNA, ESCHERICHIA
 COLI (2508)
 MORRIS HEPATOMAS, TRANSFER RNA (2512)
 NEOPLASTIC HAMSTER TISSUES, TRANSFER
 RNA METHYLASE (2088)
 RNA, DNA, 1-PHENYL-3,3-DIMETHYL-
 TRIAZENE (1762)
 RNA METHYLASE, ENZYMES, MALIGNANCY
 (2474)
 TRANSFER RNA METHYLASES, CANCER,
 REVIEW (0831)
 TRNA, DIFFERENTIATION, NEOPLASIA,
 REVIEW (2147)
 TRNA, HYPERMETHYLATION, DIMETHYLSUL-
 FATE (0319)
 TRNA, MAMMARY TUMOR, MOUSE (2506)
 TRNA, NEOPLASIA, MICE (1200)
 TRNA, NEOPLASTIC CELLS (2507)
 ETHYL AZOXYMETHANOL-ACETATE
 DNA, LIVER (0427)
 -METHYLBENZ(A)ANTHRACENE
 LIVER, ADRENAL (0066)
 ETHYL BUTYLNITROSAMINE
 NOSE, CARCINOMA, RAT (2265)*
 ETHYLCHOLANTHRENE
 FIBROSARCOMAS, MONSTROCELLULAR SARCOMA
 (1342)
 LIPOSARCOMA, IMMUNOTHERAPY, GUINEA
 PIG (1984)
 MAMMARY TUMOR VIRUS, NODULE OUTGROWTH
 LINE D BALB/C (0076)
 SARCOMA, TRANSPLANTATION ANTIGENS,
 GUINEA PIG (1985)
 SKIN SUSCEPTIBILITY, CIRCADIAN RHYTHM,
 MITOSIS, MICE (0074)
 -METHYLCHOLANTHRENE
 AGE DEPENDENCE, CARCINOGENESIS, MOUSE,
 RAT (0436)
 ANTIGENIC SPECIFICITY, DIFFERENTIAL
 ANTIGENICITY SARCOMAS (0942)
 ANTILYMPHOCYTE SERUM, MICE, IMMUNO-
 SUPPRESSION (1540)
 ASCITIC SARCOMA, CYTOGENETICS, HAMSTER
 (1219)
 BACILLUS CALMETTE-GUERIN, MOUSE
 (2272)*
 BENIGN AND MALIGNANT TUMORS, NORMAL
 MOUSE EPIDERMIS, UREA-EXTRACTABLE
 ANTIGENS (0726)
 BENZO(A)PYRENE HYDROXYLASE, PUROMYCIN,
 MICROSOMES (1805)
 BIOSYNTHESIS OF BILE ACIDS (0462)
 CARBON TETRACHLORIDE, HEPATIC LESIONS
 (0945)
 CARCINOGEN BINDING IN RAT LIVER
 (1341)

CARCINOGENESIS, MICE, SKIN, DNA,
 COLLAGENASE (1343)
 CHROMATIN, RAT LIVER NUCLEI, RNA
 SYNTHESIS (0463)
 CHROMATIN PROTEINS, NACL EXTRACTABLE,
 RAT LIVER (1337)
 CUCARCINOGEN, CANDIDA ALBICANS GLYCO-
 PROTEIN, RODENT (1801)
 CYTOCHROME P-450, PHENOBARBITAL, RAT
 (0464)
 CYTOGENETICS, MOUSE MAMMARY CARCINOMA
 (1340)
 7,12-DIMETHYLBENZANTHRACENE, ARYL
 HYDROCARBON HYDROXYLASE, MOUSE,
 ESTRADIOL (0891)
 DIMETHYLNITROSAMINE DEMETHYLASE,
 CARBOHYDRATE REPRESSION (0474)
 DNA, MAMMARY TUMORS, MURINE (1802)
 ENHANCEMENT OF TUMOR GROWTH, MURINE
 SARCOMA (1986)
 EPIDERMIZATION, UTERUS, MICE (1804)
 ERYTHROPOIETIN, SKIN TUMOR, MOUSE
 (2233)
 FIBROSARCOMA, BENZO(A)PYRENE, PRO-
 SIMIANS (0073)
 FREUND ADJUVANT, IMMUNOLOGY, RAT
 (2232)
 GLUTAMATE, SUCCINATE, LACTATE,
 ISOCITRATE, GLUCOSE-6-PHOSPHATE
 DEHYDROGENASE, MOUSE (0469)
 GUM ARABIC, BOVINE SERUM, GUINEA PIG
 (0946)
 IMMUNOLOGICAL SURVILLANCE, MICE
 (2424)
 INTERACTION WITH MOUSE EPIDERMIS,
 BIOELECTROMETRIC MEASUREMENT (0075)
 LECITHIN, CHOLESTEROL (1338)
 LIPOSARCOMA, RNA TRANSFERRED IMMUNITY
 (0077)
 LIVER CHROMATIN TEMPLATE ACTIVITY
 (0071)
 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE,
 LIVER, RAT (1786)
 MUCOUS LUBRICATION, CERVIX, MOUSE
 (2235)
 MURINE SARCOMA, COMMON ANTIGENICI-
 TIES (0468)
 MURINE SARCOMA, TUMOR SPECIFIC ANTIGEN
 (0072)
 PHENOBARBITAL, LIVER, RAT (2237)
 POLYADENYLIC-POLYURIDYLIC ACID,
 SARCOMA, MICE (2403)
 PULMONARY ADENOMATA, MICE (1806)
 RAT ETHANOL METABOLISM (0119)*
 RAT LIVER, DIMETHYLNITROSAMINE
 DEMETHYLASE INHIBITION (0466)
 RAT SKIN, BENZO(A)PYRENE HYDROXYLASE
 (0939)
 SARCOMA, LYMPH NODE CELL, MOUSE (0471)
 SARCOMA, RESPONSIVENESS, PHYTO-
 HEMAGGLUTININ, MICE (2435)
 SARCOMA, TRANSFER OF TUMOR RESISTANCE,
 RAT (1983)
 SARCOMA IN MICE, ANTITUMOR ANTIBODIES
 (0943)
 SKIN MORPHOLOGY, MOUSE (2189)
 SKIN SARCOMATA, OXYGEN CONSUMPTION
 (0465)

- SKIN TUMOR, EFFECT OF VITAMIN B12, MOUSE (2234)
 SKIN TUMORS, RAT (0470)
 SPECTROPHOTOMETRY, BLADDER WALL, RAT (0948)
 SQUAMOUS CELL CARCINOMA, LEUKEMIA IN MICE (0949)
 STOMACH CANCER, INDUCTION, SPECIFIC LOCATION (0947)
 SYNGENIC LIVER CELLS, TUMOR INHIBITION (0079)
 THYROIDITIS INDUCTION (0944)
 TUMOR, BCG VACCINE, LIVER, SPLEEN, RAT (2238)
 TUMOR, CHROMOSOME, HAMSTER (2236)
 TUMOR TRANSPLANTATION, INHIBITION OF IMMUNE RESPONSE (1551)
 20-METHYLCHOLANTHRENE
 SARCOMA, METASTASIS, MOUSE (0078)
 2-METHYL-4-DIMETHYLAMINOAZOBENZENE
 ENZYME DIETARY INDUCTION (0051)
 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE
 AMINOAZO DYE-BOUND PROTEIN (0431)
 BILE ACID, RAT (2213)
 CHLORAMPHENICOL, RAT HEPATOCARCINOGENESIS (1316)
 DIETARY INDUCTION OF ENZYMES, HEPATOCARCINOGEN (0052)
 ENZYME DIETARY INDUCTION (0051)
 HEPATO CARCINOMA, AS-300, RAT (0429)
 HYPERPLASTIC NODULE, LIVER, RAT (0430)
 LIVER, BINDING, RAT (2211)
 LIVER H PROTEIN, MOUSE (0053)
 3-METHYLCHOLANTHRENE, LIVER, RAT (1786)
 SOLUBLE MACROMOLECULES, RAT LIVER TUMORS (1317)
 TRANSPLACENTAL EFFECTS, PARTIAL HEPATECTOMY, RAT (0987)*
 METHYLETHYLNITROSAMINE
 CARCINOGENIC MECHANISM, ELECTRONIC CONSIDERATIONS (0472)
 N-METHYL-N'-NITRO-N-NITROSOGUANIDINE
 EMBRYONIC LUNG CELL CULTURE, HUMAN, CELL CYCLE, CHROMOSOME (0484)
 EXCISION OF METHYLATION PRODUCTS, E. COLI DNA (0485)
 MITOSIS, HAMSTER CELLS (2250)
 MOUSE GASTRIC CYSTS, LEIOMYOSARCOMA (1354)
 SKIN, MOUSE (2253)
 STOMACH, ULCERS, CANCER (0093)
 VAGOTOMY, SPLANCHNICOTOMY, STOMACH TUMOR, RAT (2251)
 N-METHYL-N-NITROSO-N'-ACETYLUREA
 PYLORUS, GASTRIC ADENOMA, RAT (0483)
 METHYL-NITROSOBIURET
 CANCER, STOMACH, RAT (2252)
 N-METHYL-N-NITROSO-B-D-GLUCOSYLAMINE
 GALACTOSYLAMINE, ANALOGUE, CARCINOGENICITY, RAT (2244)
 METHYLNITROSOUREA
 BLOOD BRAIN BARRIER, PERMEABILITY, CNS TUMORS, RAT (1822)
 BRAIN TUMORS, MORPHOLOGY, RAT (0963)
 MALIGNANT LYMPHOMA, DOSE AND SCHEDULE EFFECTS, MICE (0088)
 METHYLNITROSOURETHAN, RAT GASTRIC TUMORS (1823)
 N-METHYL-N-NITROSOUREA
 FORMATION OF CARCINOGEN IN RAT STOMACH, N-METHYLUREA (1820)
 NERVE TUMORS, RATS (0965)
 TISSUE DISTRIBUTION, RAT (2249)
 1-METHYL-1-NITROSOUREA
 PHENYL-DIMETHYL-TRIAcene, NEURINOMA, LACTATE DEHYDROGENASE, RAT (0966)
 METHYLTHIOURACIL
 L-THYROXINE, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, RAT (1790)
 6-METHYLTHIOURACIL
 MAMMARY GLAND CANCER, HYPOTHYROIDISM, HYPERESTRINISM, RAT (0886)
 MICROBODY
 MORRIS HEPATOMA, ENZYME (2545)
 MICROORGANISM
 CLOSTRIDIA, IMMUNOSUPPRESSION, CARCINOGENESIS, LEUKEMIA, REVIEW (1286)*
 MALIGNANCY, CANCER ISOLATE (2119)
 NEOPLASMS, ISOLATES (2121)
 URINE, CRYPTOCIDES, TUMOR ISOLATES (2120)
 MICROSOME
 BENZO(A)PYRENE HYDROXYLASE, 3-METHYLCHOLANTHRENE, PUROMYCIN (1805)
 LIVER, DIMETHYLAMINOAZOBENZENE METABOLITES, DNA BINDING (0921)
 POLYCYCLIC HYDROCARBONS, CYTOCHROME P1-450, ENVIRONMENT, RAT (1344)
 MIGRATION
 LEUKOCYTES, CARCINOMA EXTRACTS, INHIBITION (2452)
 LYMPHOMA CELL (2314)
 MILK
 DNA POLYMERASE, RNA, HUMAN (1878)
 LACTATING HAMSTERS, TUMOR INDUCTION IN OFFSPRING, DIETHYLNITROSAMINE (1813)
 MINERAL OIL
 OCCUPATIONAL EXPOSURE, CARCINOMA OF THE SCROTUM (0859)
 PARAFFINOMA, SCLEROSING LIPOGRANULOMA (1860)
 PLASMA CELL GRANULOMA, VIRUS-LIKE PARTICLES (0396)
 TUMORIGENESIS, SUSCEPTIBILITY, IMMUNE RESPONSE (0894)
 MITOCHONDRIA
 ANNULATE LAMELLAE, PARATHYROID ADENOMA (1246)
 DNA, TOPOGRAPHY, LEUKEMIA, FLOTATION DENSITY (1270)
 DNA SYNTHESIS, POLYOMA VIRUS (1513)
 MELANOMA, LIVER, AMINO ACIDS, HAMSTER (2540)
 MEMBRANE PROTEIN, LIVER, HEPATOMA, RAT (1652)
 PHOSPHORYLATION, ETHIONINE, S-ETHYL-L-CYSTEINE, LIVER, RAT (2192)
 RIBOSOMES, HELA CELLS (2528)
 TUMOR, RESPIRATORY IMPAIRMENT, ULTRA-STRUCTURE, ALTERATION (1731)
 MITOMYCIN C
 SV40, OTHER AGENTS (0660)
 TRANSFORMED MOUSE KIDNEY CELLS,

5-BROMODEOXYURIDINE, GENETIC CHANGE (0664)

OSIS

ABERRATIONS, RAT BONE MARROW, X-IRRADIATION (1844)

AROMATIC AMINES, YEAST CELLS, GENETIC ACTIVITY (0412)

BLOCK, PHYTOHEMAGGLUTININ STIMULATION, CELL DEATH, RADIATION (1136)

CELL CULTURES, MORPHOLOGY, MOLONEY VIRUS, ANTIGEN (1473)

CELL CULTURES IN VITRO, BURKITT'S LYMPHOMA, PHYTOHEMAGGLUTININ (0730)

CYCLIC AMP, BONE MARROW, THYMUS, RAT (0818)

HUMAN MELANOMA, GOLGI APPARATUS (0786)

INDEX, NEUROBLASTOMA CELLS, CELL PROLIFERATION (1242)

INHIBITION, CELL CULTURE, 6,4-BENZ-PYRENE, LUNG, RAT (0460)

LIVER CELLS, N-2-FLUORENYLACETAMIDE, L-ASPARAGINASE (1303)

MALIGNANT CELLS, CELLULAR TRANS-MEMBRANE ELECTRICAL POTENTIAL (1677)

M-METHYL-N'-NITRO-N-NITROSOGUANIDINE, EMBRYONIC LUNG CELL CULTURE, HUMAN (0484)

N-METHYL-N'-NITRO-N-NITROSOGUANIDINE, HAMSTER CELLS (2250)

MOUSE DUODENAL EPITHELIUM, GAMMA-IRRADIATION (0123)

PROLACTIN, RAT MAMMARY GLAND (1676)

RIA, DNA, CHROMOSOMES, REVERSION (2072)

SODIUM, DNA SYNTHESIS, TRANSMEMBRANE POTENTIAL, ONCOGENESIS (1269)

RBIDITY

CANCER, ALL SITES, MORTALITY RATES (0279)

PULMONARY CANCER INCIDENCE, SARDINIA (0766)*

RPHOLOGY

EPITHELIUM, CERVIX UTERI, CARCINO-GENESIS, HUMAN (0853)

MALIGNANCY RELATED CYTOLOGIC CHANGES, PERIPHERAL BLOOD SMEARS (0340)*

PULMONARY ADENOMATOUS CHANGE, BRONCHOALVEOLAR CARCINOMA (2139)

SARCOMA, AVIAN LEUKOSIS, CELL PARTICLE (0324)

THYMUS, CANCER AT VARIOUS SITES, REVIEW (1271)

TRANSITIONS, LYMPHOMA, LYMPHOCYTES IN CULTURE (1257)

RTALITY

CANCER MORTALITY DATA, NON-PUERTO RICAN WHITE POPULATION, NEW YORK CITY (0296)*

HARVEY MURINE SARCOMA VIRUS, INTER-FERON (0639)

RATES, MORBIDITY RATES, CANCER, ALL SITES (0279)

OUTH

ORAL MUCOSA, DENTURE IRRITATION, INFLAMMATORY PAPILLARY HYPERPLASIA (0737)

ORAL MUCOSA, LYMPHOCYTES, LEUKOPLAKIA (1150)

MUCOSUBSTANCE

SULFATED, COLONIC AND RECTAL MUCO-SUBSTANCES, CARCINOMA (2066)

MUTAGENESIS

AFLATOXIN B1, DROSOPHILA (2208)

ARABIDOPSIS PLANT, HEAVY ION IRRADIA-TION (0539)

CYCLOHEXYLAMINE, LEUKOCYTES (2203)

HUMAN LYMPHOCYTES, BLASTOGENESIS IN HUMAN LYMPHOCYTES, ADRIAMYCIN (0699)

MUTAGENICITY

CARCINOGEN, BACTERIOPHAGE T4 (0400)

MUTATION

ADENOVIRUS 5, TEMPERATURE SENSITIVITY, 5-BROMODEOXYURIDINE (2327)

CHROMOSOME, DIMETHYLBENZANTHRACENES, DROSOPHILA MELANOGASTER (0439)

ENVIRONMENTAL HAZARD, CHEMICAL MUTAGEN (0855)

FROG VIRUS, TEMPERATURE SENSITIVITY (2301)

GENETICS (2177)*

GENETICS, CARCINOMA, PHACOMATOSES (2583)*

LETHAL, VIRAL GENETIC MATERIAL (0864)*

MYCOBACTERIA

LEUKEMIA, TUMOR ISOLATES (2125)

MYCOBACTERIUM BOVIS

GUNIEA PIG ASCITES TUMOR, INHIBITION OF TUMOR GROWTH (0727)

MYCOPLASMA

CERVIX, SQUAMOUS CELL (0282)

CHROMOSOME ABERRATIONS, SV40 (0665)

LEUKEMICS, BLOOD DYSCRASIAS, IMMUNITY (0310)

MYCOTOXIN

ANIMALS, CANCER, STRUCTURE (1747)

HEPATIC CANCER, AFLATOXIN, NUCLEIC ACID SYNTHESIS (0849)

LEUKEMIA, MICE (1776)

STERIGMATOCYSTIN, CARCINOGENIC, LIVER CANCER, BANTU (2135)

TERATOGENESIS, CHICK EMBRYO (1779)

MYELOBLASTOSIS

SARCOMA, DNA POLYMERASE, VIRUS (1081)

VIRAL RHA, BAI AVIAN LEUKOSIS VIRUS (1890)

VIRUS, AVIAN, ANTIGEN (1967)

MYELOFIBROSIS

ACUTE, CHROMOSOME ABNORMALITY, FIBRO-BLASTIC PROLIFERATION (1247)

MYELOMA

ANTIBODIES, MOUSE TISSUE (2414)

CHROMOSOMAL ABNORMALITY, HUMAN (0797)

CHROMOSOME NUMBER ALTERATION, MSPC-1 TUMOR, MOUSE (0716)

M-COMPONENTS, ANTIGEN-BINDING IMMUNO-GLOBULINS (1736)

EPIDEMIOLOGY, LONE (0266)

GAMMA A PROTEIN (0715)

GAMMA GLOBULIN, IGG 2B, MOUSE (2005)

GAMMA 1-IMMUNOGLOBULIN, HEAVY CHAIN, PRIMARY STRUCTURE (1581)*

G-TYPE IMMUNOGLOBULINS, LIGHT AND HEAVY POLYPEPTIDE CHAINS (0226)

HAPTEN, IMMUNOGLOBULIN A (2008)

IGM DYSPROTEINEMIA, IGG, SERUM (1128)

IMMUNOGLOBULIN, LIPIDS, SERUM, MAN (2445)
 IMMUNOGLOBULIN A, HUMAN (2007)
 IMMUNOGLOBULIN IGG3, MOUSE SERUM (1568)
 IMMUNOGLOBULIN SYNTHESIS, RNA, MOUSE (2450)
 MULTIPLE, ACUTE MYELOMONOCYTIC LEUKEMIA, MELPHALAN THERAPY (0507)
 MULTIPLE, ANTIBODIES, KEYHOLE LIMPET HEMOCYANIN (1576)
 MULTIPLE, LYMPHOMA, GEOGRAPHICAL ASPECTS (0267)
 MULTIPLE, PARAPROTEIN, ELECTROPHORESIS (0333)*
 PLASMA CELL, IMMUNOGLOBULIN BIOSYNTHESIS (0720)
 PLASMACYTOMA, PROTEIN STRUCTURE, MOUSE (2006)
 PROTEIN, HAPTEN BINDING, MOUSE (2444)
 PROTEIN, HEAVY CHAIN MUTANTS, MOUSE (1564)
 PROTEIN, MEDULLARY AND EXTRAMEDULLARY PLASMACYTOMAS, IMMUNOLOGICAL REACTION (2020)*
 PROTEIN, STRUCTURE, HUMAN (2443)
 SERUM, PROTEINS (LAMBDA) (1127)
 SMOOTH MEMBRANES, ROUGH MEMBRANES, MOUSE (1667)
 SPOUSE (2535)
 SURFACE ANTIGEN, MOUSE (2415)
 MYELOPROLIFERATIVE DISEASE
 ABNORMAL CYTOLOGY (1146)
 C-GROUP CHROMOSOME, LEUKEMIC REACTION (0799)
 NOSOLOGY, PHILADELPHIA CHROMOSOME (0359)
 NAPHTHYLSISOTHIOCYANATE
 INHIBITION, DIMETHYLAMINOAZOBENZENE, LIVER, RAT (0433)
 2-NAPHTHYL N-METHYLCARBAMATE
 BETA-SEVIN, CARCINOGENICITY, RAT, MOUSE (1289)
 NASOPHARYNX
 CARCINOMA, BURKITT'S LYMPHOMA, ANTIBODY (0151)
 CARCINOMA, BURKITT'S LYMPHOMA, EPSTEIN-BARR VIRUS (1024)
 CARCINOMA, BURKITT'S LYMPHOMA, HERPES-TYPE VIRUS (1922)
 CARCINOMA, EPSTEIN-BARR VIRUS, SURFACE ANTIGEN (0579)
 CARCINOMA, HERPES-TYPE VIRUS, LYMPHO-BLASTOID TRANSFORMATION (0625)
 CARCINOMA, HUMAN, UNCLASSIFIED VIRUS (1423)
 CARCINOMA, MEMBRANE ANTIGEN, EPSTEIN-BARR VIRUS, BURKITT'S LYMPHOMA (0578)
 CARCINOMA, REVIEW (2162)
 CARCINOMA, SIBLINGS (0316)
 CARCINOMA SERUM ANTIBODY, EPSTEIN-BARR VIRUS, BURKITT'S LYMPHOMA SERUM ANTIBODY (0153)
 CERVIX, SKIN, FIBROBLASTS, CARCINOMA (1562)
 ETHMOID ADENOCARCINOMA, WOOD DUST, FURNITURE INDUSTRY (0982)

VIRUS, EPSTEIN-BARR VIRUS, CARCINOMA (2463)*
 NEGRO
 FIBROUS TISSUE SARCOMA, SOFT TISSUE SARCOMA (0273)
 NEOCARZINOSTATIN
 BURKITT'S LYMPHOMA CELLS, EPSTEIN-BARR VIRUS, VIRUS (1020)
 NEOPLASIA
 GENETICS, FANCONI'S ANEMIA, HUMAN (2534)
 NEOPLASM
 7,12-DIMETHYLBENZ(A)ANTHRACENE, SUPPLEMENTARY ASSAY (0063)
 EPIDEMIOLOGY, REVIEW (0868)*
 EPITHELIOMA, SMALLPOX VACCINE SCARS, MAN (0339)*
 MALIGNANT, EPIDEMIOLOGY, CHILD, CANADA (0755)
 OCCUPATIONAL HAZARD, OIL MIST EXPOSURE (0115)
 PRIMARY CANCER, GASTRIC STUMP, ULCER DISEASE GASTRECTOMY, MAN (0140)*
 RAT RETICULAR TUMOR, LETHAL YELLOW GENE, HEPATOMA (1198)
 RNA VIRUSES, DNA VIRUSES, REVIEW (0381)*
 TERPHENYL, REACTOR COOLANT (0111)
 TUMOR PROFILE, IMMUNOPATHOLOGICAL PROFILE, MOUSE STRAIN DIFFERENCES, REVIEW (0393)*
 NERVE
 PERIPHERAL LESIONS, RETICULOENDOTHELIAL OSIS VIRUS, MAREK'S DISEASE (0161)
 SCIATIC NERVE LESION, MAREK'S DISEASE (0158)
 SEVERANCE, TUMORIGENESIS, COCKROACH, TUMOR TRANSMISSION (1701)
 TUMORS, RATS, N-METHYL-N-NITROSOUREA (0965)
 NERVOUS SYSTEM
 DIMETHYL-SULFATE, DIETHYL-SULFATE, TUMORS (0032)
 MALIGNANCY, ETHYL-NITROSOUREA (0090)
 NEURINOMA, LACTIC DEHYDROGENASE, ISOENZYME, RATS (0966)
 TUMORS, ALDOLASE ISOZYME ACTIVITY (1255)
 TUMORS, CHILDREN, CHROMOSOMAL CHARACTERISTICS (0804)
 TUMORS, ENZYME LEVELS (1196)
 TUMORS, ISRAEL, EPIDEMIOLOGY (2485)
 TUMORS, NITROSOUREA, DESMOSTEROL (0089)
 NEURINOMA
 GASTROINTESTINAL TRACT, RECKLINGHAUSE DISEASE, SCHWANN CELLS, PATHOGENESIS (1593)
 NEUROBLASTOMA
 ACETYLCHOLINESTERASE, MOUSE (0783)
 ANTIGENS, FETUS, ADRENALS (1577)
 CELL-FREE EXTRACT, TUMOR INDUCTION (0567)
 DNA REPLICATION, HUMAN (1230)
 GANGLIONEUROMA, TURNER'S SYNDROME, NONGONADAL NEOPLASIA (0012)
 MITOTIC INDEX, CELL PROLIFERATION (1242)

TYROSINE HYDROXYLASE ACTIVITY,
 INHIBITION, HUMAN (2064)
 ULTRASTRUCTURE, ANNULATE LAMELLAE,
 HUMAN (1684)
 ROMA
 TRAUMA, ULTRASTRUCTURE (1402)*
 US
 CELLULAR BLUE, MALIGNANT INFILTRATION,
 OF BRAIN (1698)
 T TEST
 NECROSIS, ALTERED LIPIDS (0036)
 KEL
 BLOOD, URINE, EXCRETION, RAT (2268)*
 COBALT, OCCUPATIONAL EXPOSURE, CANCER
 INCIDENCE (1185)
 HAMSTER (2195)
 NASAL CANCER, LUNG CANCER, PLANT
 WORKER'S (2043)
 REVIEW (2154)
 KEL CARBONYL
 GAS, EFFECTS OF ACCIDENTAL EXPOSURE
 (0510)
 OTINAMIDE
 PANCREAS, TUMOR, RAT (2186)
 OTINE
 GASTRIC SECRETION, MUCOSAL SEROTONIN
 LEVEL, RAT, ATROPINE (0502)
 RITE
 FREE RADICAL, ANTICARCINOGEN,
 2-ACETYLAMINOFLUORENE (0042)
 4-(5-NITRO-2-FURYL)-2-THIAZOLYL)
 CETAMIDE
 STOMACH NEOPLASM, LEUKEMIA (0417)
 4-(5-NITRO-2-FURYL)-2-THIAZOLYL)
 ORMAMIDE
 URINARY CARCINOGENICITY, GALL BLADDER
 (0038)
 ITRONAPHTHALENE
 BLADDER PAPILLOMA, MONKEY (0027)
 ITROQUINOLINE-1-OXIDE
 ALVEOLAR EPITHELIAL CELLS, NUCLEOLAR
 ALTERATIONS (0491)
 4-AZOQUINOLINE-1-OXIDE, ANTIBODY TO
 CARCINOGEN (1994)
 BACTERIOPHAGE, BACTERIAL MUTANTS
 (0489)
 CARCINOGENICITY, ELECTRONIC STRUCTURE,
 REVIEW (1745)
 DNA, INTERACTION, MODEL (1825)
 DNA, NUCLEOSIDES, ELECTRON SPIN
 RESONANCE (1355)
 DNA REPAIR SYNTHESIS, CHROMOSOME
 ANOMALY, HUMAN, HAMSTER (0968)
 4-HYDROXYAMINOQUINOLINE-1-OXIDE,
 CHROMOSOME ALTERATION, HAMSTER
 EMBRYONIC CELL (0098)
 IN VIVO CARCINOGENICITY, REVIEW (1746)
 KIDNEY, RAT (2270)*
 LUNG ADENOMA, ALUMINUM (0096)
 METABOLISM, ELIMINATION, RAT (0967)
 MODE OF INCORPORATION, BINDING (0490)
 RAT LIVER CARCINOMAS, TRANSPLANTABLE
 TUMOR LINE (1824)
 RAT LIVER CELL CULTURE, ULTRASTRUCTURE
 (0094)
 SARCOMA, MICE (1357)
 SURFACTANT EFFECT, GASTRIC NEOPLASMS,
 RAT (0095)

VIRUS, DNA REPAIR SYNTHESIS (1356)
 YOSHIDA SARCOMA CELLS, CHROMOSOME
 ABERRATION, PERSISTENT NUCLEOLI
 (0097)
 NITROSAMIDES
 GASTRIC CANCER, NITROSOURETHAN,
 NITROSUREA (1819)
 NITROSAMINE
 ADENOCARCINOMA, LUNG, MOUSE (2239)
 SODIUM NITRITE, LUNG, ADENOMA, MOUSE
 (2241)
 SPINACH, CARCINOGENIC HYDROCARBONS
 (0880)*
 SUSCEPTIBILITY, GUINEA PIG (2152)
 NITROSAMINE DERIVATIVES
 RATS, HEPATOCELLULAR CARCINOMA (0435)
 NITROSOAZETIDINE
 NITROSOHEPTAMETHYLENEIMINE, STOMACH,
 LUNG (0086)
 N-NITROSOBUTYLUREA
 ASCITES TUMOR, MYELOGENOUS GRANULO-
 CYTIC LEUKEMIA (1353)
 LEUKEMOGENESIS (0091)
 MAMMARY TUMOR, LEUKEMIA, MICE, RATS
 (0092)
 N-NITROSODIETHYLAMINE
 HEPATOCARCINOMA, MONKEY,
 ULTRASTRUCTURE (0955)
 N-NITROSODIMETHYLAMINE
 TUMORIGENESIS, MASTOMYS (0958)
 NITROSOHEXAMETHYLENEAMINE
 RAT LIVER, ULTRASTRUCTURAL STUDY
 (1817)
 N-NITROSOHEXAMETHYLENEIMINE
 OROPHARYNGEAL TUMOR, FACIAL TUMOR,
 MOUSE, EPITHELIUM (0479)
 N-NITROSO-N-METHYLANILINE
 GASTROINTESTINAL TRACT, PAPILLOMA,
 CARCINOMA (0476)
 N-NITROSO-N-METHYLCYCLOHEXYLAMINE
 GASTROINTESTINAL TRACT, PAPILLOMA,
 CARCINOMA (0476)
 N-NITROSOMETHYLUREA
 ASTROCYTOMA, GLIOBLASTOMA, RAT (1991)
 ASTROCYTOMA, GLIOMAS, RAT (1821)
 N-NITROSO-N-METHYLUREA
 NEWBORN AND WEANED MICE, LYMPHOSARCOMA
 (0962)
 RESPIRATORY TRACT, EPIDERMOID
 CARCINOMA, HAMSTER (0482)
 N-NITROSO-N-METHYLURETHAN
 LUNG HISTOLOGY, ALKALINE PHOSPHATASE,
 MOUSE (0486)
 N-NITROSOMORPHOLINE
 DIMETHYLNITROSAMINE, SERINE
 DEHYDRATASE, RAT (2427)
 HEPATOCELLULAR CHANGES, GLYCOGEN
 (1818)
 NUCLEASES, LIVER, RAT (2247)
 RIBOSOMAL FERRITIN, RAT LIVER
 (0475)
 N-NITROSOPENTAMETHYLENEIMINE
 OROPHARYNGEAL TUMOR, FACIAL TUMOR,
 MOUSE, EPITHELIUM (0479)
 NITROSOPIPERAZINE
 CARCINOGENICITY, RATS (0087)
 NITROSOETHIOMORPHOLINE
 CARCINOGENICITY, RATS (0087)

NITROSOUREA
 NERVOUS SYSTEM TUMORS, DESMOSTEROL,
 RAT (0089)
 N-(BETA-CHLOROETHYL)-N-NITROSOURETHAN
 TUMOR, STOMACH, LUNG, RAT (2256)
 NOSF
 METHYLBUTYLNITROSAMINE, CARCINOMA, RAT
 (2265)*
 NASAL PAPILLOMATOSIS, HISTOLOGY, VIRAL
 ETIOLOGY (0373)
 NASAL SINUS, WOOD DUST, ADENOCARCINOMA
 (0113)
 NOSOLOGY
 PHILADELPHIA CHROMOSOME, MYELOPRO-
 LIFERATIVE DISEASES (0359)
 NUCLEIC ACID
 2-ACETYLAMINOFLUORENE, METABOLITE
 BINDING (1301)
 BASIC PROTEIN ESTIMATION, MAMMARY
 ADENOCARCINOMA (0190)
 BINDING, TUMOR INDUCTION, AFLATOXINS
 (0047)
 DISTRIBUTION, ASCITIC SARCOMA, ROUS
 SARCOMA VIRUS, MOUSE CELL (1080)
 DNA, RNA, AFLATOXINS, REVIEW (1744)
 DNA, RNA, COMPLEMENTATION (0554)
 DNA, RNA, 1-PHENYL-3,3-DIMETHYL-
 TRIAZENE, METHYLATION (1762)
 DNA, RNA, POLYMERASE, ENDONUCLEASE,
 ROUS SARCOMA VIRUS (0647)
 DNA, RNA, POLYMERASE, ONCOGENIC VIRUS
 (0553)
 DNA SYNTHESIS, RNA, LEUKEMIA (1641)
 EMBRYO, ACTINOMYCIN D, 7,12-DIMETHYL-
 BENZ(A)ANTHRACENE, 1-MERCAPTO-1-
 (BETA-4-PYRIDETHYL)BENZIMIDAZOLE
 (1322)
 FLUORENYLAMINE POLYNUCLEOTIDE, RNA,
 DNA, 2-FLUORENYLHYDROXYLAMINE (1306)
 INHIBITION, HEPATOMA, PREDNISOLONE,
 PHYTOHEMAGGLUTININ (0696)
 LIVER, N-HYDROXY-N-ACETYL-4-AMINO-
 BIPHENYL, RAT (2181)
 MAMMARY TUMOR TISSUE, 32 PHOSPHORUS
 INCORPORATION (2081)
 METHYLATION, CHEMICAL CARCINOGEN,
 DIMETHYLNITROSAMINE, METABOLISM
 (0473)
 MICROSOMAL MEMBRANE, LIVER, CHEMICAL
 CARCINOGEN, RAT (0913)
 MYCOTOXIN, HEPATIC CANCER (0849)
 NEOPLASTIC COLONIC CELLS, PROLIFERA-
 TION (2076)
 POLYRIBOINOSINIC-POLYRIBOCYTIDYLIC
 ACID, POLYOMA VIRUS, INHIBITION OF
 ONCOGENESIS (0685)
 PROTEIN SYNTHESIS, VIRUS (1426)
 RNA, DNA, CHROMOSOMES, MITOSIS (2072)
 RNA, DNA, METHYLASES (2150)
 RNA, DNA, POLYMERASE, AVIAN MYELOBLAS-
 TOSIS (0586)
 RNA, DNA, POLYMERASE, ROUS SARCOMA
 VIRUS (0651)
 RNA, DNA, SYNTHESIS, LEUKEMIA (1431)
 ROUS VIRUS, REPLICATION, CHICK EMBRYO
 CELLS (2362)
 SYNTHESIS, BINDING, ORTHO-AMINO-
 AZOTOLUENE, MOUSE LIVER (1320)

SYNTHESIS, HEPATOMA, RAT (2544)
 SYNTHESIS, INHIBITION, AFLATOXIN
 (0049)
 SYNTHESIS, LIVER REGENERATION,
 7,12-DIMETHYLBENZ(A)ANTHRACENE (008)
 SYNTHESIS, PHENOBARBITAL, AFLATOXIN
 (0919)
 SYNTHESIS, SHOPE FIBROMA VIRUS
 INFECTION, VIRUS, FOCUS FORMATION
 (0657)
 TRACHEAL PAPILLOMA, HAMSTERS, DIETHY-
 LAMINE NITROSAMINE (1349)
 URETHAN, PROTEIN, INTERACTION (1362)
 TUMOR, VX7 TYPE CARCINOMA, SHOPE VIRUS
 PAPILLOMAS (1074)
 NUCLEOLUS
 MORPHOLOGY, THYMIC LYMPHOCYTES,
 X-IRRADIATION, (1842)
 NUCLEOTIDE
 ADENINE, ENERGY, GLUCOSE, NOVIKOFF
 HEPATOMA (2539)
 ETHANOLAMINE, CHOLINE, HEPATOMA, RAT
 (1660)
 NUCLEOSIDES, HEPATOMA, GROWTH, RAT
 (2497)
 POLY I.C. VIRUS, HERPESVIRUS SAIMIRI
 INTERFERON (1918)
 NUCLEUS
 NUCLEAR BODIES, MALIGNANT TUMORS,
 BENIGN TUMORS, ELECTRON MICROSCOPY
 (1672)
 NUTRITION
 HIGH-VOLUME FEEDING, OCULAR CARCINO-
 MA IN CATTLE (0780)
 OCCUPATIONAL HAZARD
 ASBESTOS, MESOTHELIOMA, EPIDEMIOLOG
 (2481)
 BENZENE, TOLUENE, CHROMOSOME CHANGE
 (2193)
 BENZENE, TOLUENE, LEUKEMIA (1370)
 BENZENE HEXACHLORIDE, CHLOROPHENO-
 THANE, ACUTE LEUKEMIA (0509)
 BENZO(A)PYRENE, ALUMINIUM PLANT (22)
 BENZO(A)PYRENE, COKE OVEN (1800)
 BERYLLIUM, CHRONIC INTOXICATION,
 CANCER (0981)
 CANCER, 3,4-BENZOPYRENE, LARYNGEAL
 CANCER (0117)*
 CARCINOMA OF THE SCROTUM, MINERAL OIL
 (0859)
 GLASS FIBERS, LUNG CANCER, REVIEW
 (0874)*
 HEMATITE MINING, LUNG CANCER (0015)
 INORGANIC AGENTS, AZO DYES, RADIATION
 REVIEW (0878)*
 INORGANIC CARCINOGENS, RADIATIONS,
 REVIEW (0877)*
 LABORATORY WORKER, BLADDER CARCINOMA,
 CHEMICAL CARCINOGEN (0367)
 NETHERLANDS SHIPYARDS, MESOTHELIOMA,
 ASBESTOS EXPOSURE (2046)
 NICKEL PLANT WORKERS, NASAL CANCER,
 LUNG CANCER (2043)
 OIL MIST EXPOSURE, NEOPLASM (0115)
 PULMONARY FUNCTION, ASBESTOS DUST
 EXPOSURE (1857)
 RADIATION, QUARTZ, PLEURAL MESO-
 THELIOMA (0996)

RESPIRATORY CANCER, STEELWORKERS,
 COKE WORKERS, MORTALITY RATES (1369)
 SCOTLAND, MESOTHELIOMA, ASBESTOS
 (1170)
 SCROTAL CANCER, INDUSTRIAL HYGIENE
 (0116)
 SKIN CANCER, RESPIRATORY CANCER (1277)
 TOLUENE, BENZENE, ALKALINE PHOSPHA-
 TASE, LEUKOCYTE LEVEL (1374)*
 TUMORS OF URINARY BLADDER, TEXTILE
 WORKERS (0980)
 URANIUM MINERS, LUNG CARCINOMA, TISSUE
 TYPE (1859)
 WOOD DUST, ETHMOID ADENOCARCINOMA,
 FURNITURE INDUSTRY (0982)
 OPINE
 PLANT TUMORIGENESIS PROMOTERS (0404)
 NTOMA
 MIXED CALCIFIED ODONTOGENIC TUMORS,
 PATHOLOGY, CLINICAL PROFILE (0374)
 MIST EXPOSURE, NEOPLASM, OCCUPATIONAL
 HAZARD (0115)
 MIST EXPOSURE, OCCUPATIONAL HAZARD,
 RESPIRATORY TRACT CANCER (0276)
 OVERHEATED, CARCINOGENICITY,
 BENZO(A)PYRENE, RAT (2196)
 L CAVITY
 BUCCAL MUCOSA, TOBACCO CHEWING,
 BETEL-NUT (0978)
 BUCCAL POUCH, EPIDERMAL CARCINOMA,
 ANTILYMPHOCYTE SERUM, 7,12-DIMETHYL-
 BENZ(A)ANTHRACENE (1541)
 BUCCOPHARYNGEAL CANCER, CERVIX, INDIA,
 INCIDENCE (2038)
 CARCINOMA, INDIA, TOBACCO (1624)
 7,12-DIMETHYLBENZ(A)ANTHRACENE,
 MANDIBULAR LYMPHOMA (1788)
 FACE, TUMORS, EPIDEMIOLOGY,
 CZECHOSLOVAKIA (2484)
 HISTOLOGY OF BUCCAL MUCOSA, TOBACCO
 CHEWING, BETEL-NUT CHEWING (0979)
 OKAL AND OROPHARYNGEAL CANCER, INDIA,
 TOBACCO CHEWING (1177)
 RADIATION, VERROUS EPIDERMAL CARCINOMA
 ANAPLASTIC TRANSFORMATION, HUMAN
 (0131)
 SQUAMOUS CELL CARCINOMA, CANINE
 PAPILLOMATOSIS (1151)
 L CONTRACEPTIVE
 CANCER INCIDENCE (1743)
 CERVICAL CANCER, CERVICAL DYSPLASIA
 (0281)
 CERVICAL HYPERPLASIA (2478)*
 CHROMOSOME ABNORMALITIES (0503)
 DEPO-MEDROXYPROGESTERONE ACETATE,
 CERVICAL MALIGNANCY (1832)
 MAMMARY CANCER, ANIMALS, UTERINE
 CERVICAL CANCER (1742)
 MAMMARY CARCINOMA (0984)
 MAMMARY COMEDOCARCINOMA, HISTOLOGICAL
 EXAMINATION (0505)
 MULTIPLE MAMMARY FIBROADENOMAS (1378)*
 SEQUENTIAL, CYTOLOGIC ABNORMALITIES,
 CARCINOMA IN SITU (0504)
 SAN TRANSPLANTATION
 BRAIN MESENCHYMAL TUMORS, HUMAN (2138)
 LYMPHORETICULAR NEOPLASM, IMMUNO-

SUPPRESSION, ANTIGEN, HYPERPLASIA
 (1589)
 ORTHOAMINOAZOTOLUENE
 BINDING, LIVER CELLS, NUCLEIC ACID
 SYNTHESIS (1320)
 LIVER, BIOMYCIN, MOUSE (0025)
 OSTEOSARCOMA
 BONE MARROW, STRONTIUM -90 (1381)
 7,12-DIMETHYLBENZ(A)ANTHRACENE,
 SYNESTROL, RABBIT (1329)
 FELINE SARCOMA VIRUS, TRANSFORMATION,
 HUMAN (2298)
 MOLONEY VIRUS, RAT (0637)
 RADIUM POISONING, LYMPHOMYELOID
 CARCINOMA (0001)
 ULTRASTRUCTURE, TUBULAR STRUCTURES
 (2565)
 OVARY
 ASCITES TUMOR, SULFANILIC ACID-
 CONJUGATED ANTIGENS, RAT (0732)
 CANCER, UNITED STATES INCIDENCE,
 UTERINE CANCER (1619)
 CYSTADENOCARCINOMA, CERVICAL SQUAMOUS
 CELL CARCINOMA, TS ANTIGENS (2000)
 FAMILIAL OVARIAN CARCINOMA, PAPILLARY
 ADENOCARCINOMA, GENETIC PREDISPOSI-
 TION (0808)
 IONIZING RADIATION, TUMORIGENESIS,
 MOUSE (1845)
 NEOPLASIA, DNA, CHROMOSOME, HUMAN
 (2536)
 OVARIECTOMY, TUMOR REGRESSION,
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 (1327)
 RADIATION EXPOSURE, CHORIONIC GONADO-
 TROPIN, ANDREOBLASTOMA (1594)
 RAT CORPORA LUTEA, STEROIDOGENESIS,
 ANILINE (1319)
 THECOMA, ANTICONVULSANT CHEMOTHERAPY
 (1371)
 TUMORS, 7,12-DIMETHYLBENZ(A)ANTHRACENE
 METABOLISM, MICE (1787)
 TUMORS, GENETIC MOSAICISM, GONADO-
 BLASTOMA (1689)
 UTERUS, MAMMARY GLAND, CARCINOMA,
 IMMUNOLOGY (1135)
 OVUM
 SV40, MOLONEY SARCOMA VIRUS (1931)
 OZONE
 LUNG, NEOPLASIA, MICE (0884)
 PAGET'S DISEASE
 X CHROMOSOME, SIMIAN VIRUS 40 (0245)
 PAINT
 PAINT REMOVERS, CARCINOMA, PENIS
 (0114)
 PALMOTOXIN
 EMBRYO LIVER, AFLATOXIN (0425)
 PANCREAS
 CANCER, DIABETES MELLITUS (1244)
 CANCER, DIABETES MELLITUS, CANCER
 INCIDENCE AND MORTALITY, REVIEW
 (1724)
 CANCER, MORTALITY RATES, CIGARETTE
 SMOKING (1178)
 CANCER EPIDEMIOLOGY, NEGRO (2479)
 HAMSTER ISLET CELL TUMORS, DOPA,
 TYROSINE HYDROXYLASE ACTIVITY
 (1222)

ISLET CELL TUMOR, PYRROLIZIDINE
ALKALOID (0033)
PANCREATIC ISLET CELL ADENOMA, ULTRA-
STRUCTURAL STUDY (2105)
TUMOR, NICOTINAMIDE, STREPTOZOTOCIN,
RAT (2186)
PANTOTHENIC ACID
DEFICIENCY, FOCAL AVILLOUS HYPERPLASIA
MOUSE DUODENUM (0311)
PAPILLOMA
CANINE, SQUAMOUS CELL CARCINOMA, ORAL
CAVITY (1151)
FORESTOMACH, URETHAN, HAMSTER (0100)
INFRARED EMISSION (0354)*
LYMPHOMA, PAPOVA VIRUS, HAMSTER (1956)
PHORBOL ESTER ACETATE, 7,12-DIMETHYL-
BENZ(A)ANTHRACENE (1321)
SHOPE VIRUS, Vx7 TYPE CARCINOMA,
NUCLEIC ACID (1074)
PARASITE
CANCER, BILHARZIASIS, BLADDER, NERVOUS
SYSTEM, TOXOPLASMOSIS (1727)
NEMATODE INFECTION, TUMOR GROWTH,
IMMUNITY TO PARASITE (2118)
PARATHYROID
ADENOMA, ANNULATE LAMELLAE, MITO-
CHONDRIA (1246)
ADENOMA, ULTRASTRUCTURE, CILIA (1669)
THYROID, HUMAN, IODINE, HUMAN (1635)
PAROTID GLAND
MIXED TUMOR (0530)
TUMOR, EPITHELIAL ORIGIN, HUMANS
(2033)*
TUMOR, GROWTH RATE, 32P ACCUMULATION
(1634)*
PATHOGENESIS
AMERICUM 241, HISTOLOGICAL DISTRIBUTION
IN RAT (1016)*
CARCINOMA, MAMMARY GLAND, REVIEW
(1757)*
CARCINOMA OF RECTUM, MUCOSAL FOLDS,
PERILESIONAL CHANGES (1592)
HORMONE-PRODUCING TUMOR, ADRENAL
CORTEX, REVIEW (2161)
KIDNEY TUMOR, SYNESTROL, HAMSTER
(1586)
LARYNX, ELECTRON MICROSCOPY, LIGHT
MICROSCOPY (1152)
LYMPHOPROLIFERATIVE DISORDERS, IMMUNE
DEFICIENCY, REVIEW (1760)*
NEOPLASIA, PULMONARY TUBERCULOSIS
(2472)
NEOPLASM, ENZYME, MODIFICATION
PROCESSES, REVIEW (0860)
OVARIAN TUMOR, RADIATION EXPOSURE,
MOUSE (1845)
PRECANCEROUS STATE, ESOPHAGITIS,
CICATRITION, PEPTIC STENOSIS (0851)
PULMONARY LYMPHANGIOSIS, METASTASIS,
HUMAN (2473)
THYROID CANCER, ADENOMA, GOITER,
HUMANS (2030)
TUMOR, PAROTID, EPITHELIAL ORIGIN,
HUMANS (2033)*
TUMOR, RENAL PELVIS, CORAL CALCULUS
(1600)*
URINE BLADDER TUMOR, DARK CELLS,
HUMANS (2028)

UTERINE CARCINOMA, REVIEW (0852)
PATHOLOGY
IMMUNOGENICITY, MURINE SARCOMA VIRUS
(1472)
SPONTANEOUS, LEUKEMIA, FISCHER, RAT
(0323)
TUMOR, MALIGNANT, MORPHOLOGY (2165)*
PENIS
CARCINOMA, PAINT, PAINT REMOVERS
(0114)
PERIODATE
INDUCTION OF LYMPHOCYTE TRANSFORMATION
(1377)*
PESTICIDES
ALDRIN, DIELDRIN, ENDRIN, TUMOR-
IGENICITY (0421)
CIGARETTE TOBACCO, TUMOR PROMOTION
(1793)
ENVIRONMENTAL HUMAN CANCER, FOOD
ADDITIVES (1275)
RENAL ADENOCARCINOMA, LEOPARD FROGS
(0896)
SEVIN, MANEB, CIRAM, CINEB, CARCINO-
GENICITY, RAT (1290)
PETROLEUM
PRODUCT, BAYOL F, PLASMACYTOMA INDUC-
TION, ANTITHYMOCYTE SERUM (0691)
PETS
CHILDHOOD LEUKEMIA, DOG BITES (2133)
DOMESTIC CATS, CHILDHOOD LEUKEMIA,
EXPOSURE (1604)
DOMESTIC CATS, HUMAN LYMPHOMA, HOUSE-
HOLD QUESTIONNAIRE SURVEY (1182)
FELINE FIBROSARCOMA, TUMOR INDUCTION
IN MAMMALS (1872)
FELINE LYMPHOMA, VIRUS, SARCOMA (144)
PHACOMATOSES
MUTATION, GENETICS (2583)*
PHAGOCYTOSIS
IODINE, LEUKEMIA, HUMAN (2063)
PHARYNX
HYPOPHARYNX, CARCINOMA, RADIATION
EXPOSURE (0995)
PHENANTHRENE
K-REGION EPOXIDE, DIBENZ(A,H)ANTHRA-
CENE, DNA, RNA (0067)
PHENOBARBITAL
AFLATOXIN B1, LIVER NUCLEIC ACID
SYNTHESIS (0919)
CYTOCHROME P-450, 3-METHYLCHOLANTHRE-
NOL (0464)
LIVER, 3-METHYLCHOLANTHRENE, RAT (22)
URETHAN CARCINOGENESIS, LUNG, MOUSE
(0493)
PHENOL
DERIVATIVES, STRUCTURE-ACTIVITY
RELATIONS, HAMMETT-TAFT EQUATION,
REVIEW (0347)
PHENOLPHTHALEIN
MELANOMA, CARCINOMA, B-GLUCURONIDASE
MOUSE (2085)
1-PHENYL-3,3-DIMETHYLTRIAZENE
RNA, DNA, METHYLATION (1762)
PHEOCHROMOCYTOMA
FAMILIAL, MEDULLARY THYROID CARCINOMA,
CALCITONIN ACTIVITY (0803)
FAMILIAL VON HIPPEL-LINDAU'S DISEASE
(0828)*

ILADELPHIA CHROMOSOME
 NGSOLOGY, MYELOPROLIFERATIVE DISEASES
 (0359)
 LEOMYCIN
 ESTER ACETATE, PAPILLOMA,
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 (1321)
 POLYOMA, VIRUS SYNTHESIS IN VITRO
 (1511)
 ORBOL
 LEUKEMOGENESIS, 7,12-DIMETHYLBENZ-
 (A)ANTHRACENE (0893)
 MYRISTATE ACETATE, INDUCED VASCULAR
 CHANGES (0398)
 13-O-TETRADECANOYL-PHORBOL-12-ACETATE,
 THYMIDINE INCORPORATION, CROTON OIL
 (0892)
 TRITIUM LABELING TECHNIQUE, CROTON OIL
 (0516)*
 OSPHOLIPID
 HEPATOMA CELLS, CALCIUM, MAGNESIUM,
 MEMBRANE (1651)
 SYNTHESIS, POLYOMA VIRUS, HAMSTER
 CELLS (1514)
 TURNOVER, NEOPLASTIC MAST CELL (0256)
 OTOCARCINOGENICITY
 AROMATIC HYDROCARBON, MECHANISM (0345)
 YTOHEMAGGLUTININ
 BURKITT'S LYMPHOMA, CELL CULTURES IN
 VITRO, MITOTIC INDEX (0730)
 CONSUMPTION, LYMPHOCYTES, HODGKIN'S
 DISEASE (0733)
 DNA SYNTHESIS IN LYMPHOCYTES, EXTRA-
 CORPOREAL IRRADIATION OF BLOOD
 (0526)
 FOLATE UPTAKE, HUMAN LYMPHOCYTES
 (0701)
 HUMAN LYMPHOCYTE, ROLE OF ERYTHROCYTE
 (1571)
 HUMAN LYMPHOCYTE AGGREGATE ENZYME,
 RNA SYNTHESIS (1138)
 HUMAN LYMPHOCYTE BLASTOGENESIS,
 PROTEIN ACCUMULATION (0697)
 LOW TEMPERATURE STORAGE, LYMPHOCYTE
 (0237)
 LYMPHOCYTE, CANCER PATIENTS,
 ALLOGENEIC PLASMA (2460)
 LYMPHOCYTE, CYCLIC AMP, TRANSFORMATION
 (0236)
 LYMPHOCYTE, HEME-SYNTHESIS, HEMA-
 TOPOIETIC HUMORAL FACTORS (0700)
 LYMPHOCYTE, IMMUNITY (1137)
 LYMPHOCYTE, PROLIFERATION, LYMPH-
 ADENOSIS, LYMPHOGRANULOMATOSIS
 (1720)*
 LYMPHOCYTE DEDIFFERENTIATION,
 DYNAMICS, MICROKINEMATOGRAPHY, MAN
 (0243)*
 LYMPHOCYTE RESPONSE, DOWN'S SYNDROME
 (1570)
 LYMPHOCYTE TRANSFORMATION, CANCER
 PATIENTS (1998)
 LYMPHOCYTE TRANSFORMATION, CYCLIC AMP
 (0702)
 LYMPHOCYTE TRANSFORMATION, DNA POLY-
 MERASE, REPLICATION (0703)
 LYMPHOCYTE TRANSFORMATION, LYMPHOMA,
 CELL CULTURE (0239)

MEGALOBLASTIC ANEMIA, MORPHOLOGY,
 DNA SYNTHESIS (0698)
 MITOTIC BLOCK, CELL DEATH, RADIATION
 (1136)
 P, MONONUCLEAR CELLS, PERITONEAL
 FLUID (1572)
 PISUM SATIVUM L., ERVUM LENS L.,
 LYMPHOBLASTIC TRANSFORMATION, IN
 VITRO, MAN (0242)*
 RAT LYMPH NODE CELLS, NONSPECIFIC
 ANTIBODY, SV40 (1097)
 RNA SYNTHESIS, DNA SYNTHESIS, HEPATOMA
 (0696)
 SPLEEN, THYMUS, LYMPH NODES (1122)
 THYMUS, MICE (1573)
 TRANSFER RNA METHYLASE ACTIVITY,
 CHRONIC LYMPHOCYTIC LEUKEMIA (2091)
 TRANSFORMATION, HUMAN LYMPHOCYTES,
 AFLATOXIN B (0045)
 PINEAL BODY
 MELANOID TUMORS, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, GOLDEN HAMSTERS, SEX
 (1328)
 PINGUECULA
 AFRICAN PATIENTS, CONJUNCTIVAL LESIONS
 (1213)
 PITUITARY
 CHOLESTEROL-RICH DIET, LIPID-RICH
 DIET, NEOPLASMS, LUNG (0397)
 PLACENTA
 ANEMIA-INDUCING SUBSTANCE, MUCOPROTEIN
 IN URINE OF CANCER PATIENTS, COMMON
 ANTIGENICITY (1575)
 BENZO(A)PYRENE, KIDNEY, MOUSE (2231)
 CHORIOCARCINOMA, KIDNEY (2014)
 HUMAN CHORIOCARCINOMA, TROPHOBLASTIC
 TUMOR CELLS, HORMONE SYNTHESIS
 (1653)
 3'-METHYL-4-DIMETHYLAMINOAZOBENZENE,
 PARTIAL HEPATECTOMY, RAT (0987)*
 TRANSPLENTAL EFFECT, DIMETHYLNITRO-
 SAMINE, NEOPLASM (0477)
 PLANT
 ARABIDOPSIS, HEAVY ION IRRADIATION,
 MUTAGENESIS (0539)
 POLYCYCLIC HYDROCARBONS, AIR
 POLLUTANTS, FOOD (0397)
 PROMOTER, OCTOPINE, LYSOPINE (0404)
 SENEIO LONGILOBUS, HEPATOCARCINOMA
 (1293)
 PLASMA
 CELL TUMOR, FREUND'S ADJUVANT (0395)
 CELL TUMOR, IMMUNOGLOBULIN, CARBO-
 HYDRATE, BIOSYNTHESIS, MOUSE (1565)
 LEUKEMIC PLATELETS, CHRONIC MYELOID
 LEUKEMIA, ADENOSINE DEAMINASE
 ACTIVITY (1643)
 MYELOMA, IMMUNOGLOBULIN BIOSYNTHESIS
 (0720)
 PLASMACYTOMA
 ASCITES TUMOR JB-1, MOUSE (0824)
 CELL CULTURE OF TUMOR, IMMUNOGLOBULIN
 PRODUCTION, MURINE (1546)
 FREUND'S ADJUVANT, MICE (0394)
 INDUCTION, ANTITHYMOCYTE SERUM,
 BAYOL-F (0691)
 MURINE, CELL DIFFERENTIATION, IN VITRO
 (0819)

- PROTEIN STRUCTURE, MYELOMA, MOUSE
(2006)
SERUM PARAPROTEIN (0729)
- POLLUTION
BENZO(A)PYRENE, FIBROSARCOMA, MOUSE
(2258)
CHEMICAL CARCINOGENS, TERATOGEN
(0518)*
- POLONIUM
RADIOACTIVITY, TOBACCO SMOKE, REVIEW
(0332)*
- POLYCYCLIC HYDROCARBONS
CELL TRANSFORMATIONS, HAMSTER (2197)
- POLYCYCLIC THIAZOLE
CARCINOGENS (2269)*
- POLYCYTHEMIA
CHROMOSOME ABERRATIONS, HUMAN (2531)
PHILADELPHIA CHROMOSOME, CHRONIC
MYELOID LEUKEMIA (0010)
TRANSFUSION, HYPOXIA, ERYTHROPOIETIN
(0307)
VERA, GRANULOCYTE, MURAMIDASE (0320)
VERA, JEWISH POPULATION, INCREASED
RISK OF MALIGNANCY (1615)
- POLYINOSINIC-POLYCYTIDYLIC ACID
LYMPHOMA, THYMUS, 7,12-DIMETHYLBENZ-
(A)ANTHRACENE, MOUSE (2225)
- POLYNUCLEOTIDE
POLYADENYLIC-POLYURIDYLIC ACID,
3-METHYLCHOLANTHRENE, SARCOMA, MICE
(2403)
- POLYPS
ADENOMATOUS, SOUTH AFRICAN BANTU,
CARCINOMA OF THE LARGE BOWEL (0759)
CARCINOMA, STOMACH (2569)
CERVIX, HYPERESTRINISM, ENDOMETRIAL
HYPERPLASIA (0742)
GASTRIC MUCOSA, ADENOMATOUS (1155)
JUVENILE, COLON AND RECTUM (1591)
JUVENILE, COLON, ALLERGY, FAMILIAL
(0326)
- POLYRIBOSOME
CYTOPLASMIS, PROTEIN SYNTHESIS,
EHRlich'S TUMOR (2529)
SPLEEN, RAUSCHER VIRUS, MOUSE (0607)
- POLYSACCHARIDE
MUCOSUBSTANCES, CANINE MASTOCYTOMA
(0329)
- POLYVINYLPYRIDINE-N-OXIDE
LUNG TUMORS IN RATS, INHALATION OF
CARCINOGEN (1768)
- PRECANCEROUS CONDITION
CERVIX, CHROMOSOME, HUMAN (2467)
MALIGNANT TRANSITION, CERVIX UTERI,
HISTOCHEMICAL CHANGES (1595)
MELANOSIS, STALE EPHELIDE (2026)
SERUM PROTEIN CONCENTRATIONS, ANTIGEN-
SENSITIZED MICE (1587)
SQUAMOUS CELL CARCINOMA, SUBMUCOUS
FIBROSIS (0247)
UTERUS, SEX CHROMATIN, CYTOLOGY,
HUMANS (1596)
- PREDNISOLONE
MOLONEY LEUKEMIA VIRUS, LEUKEMIA,
THYMUS (0173)
MURINE LEUKEMIA VIRUS, THYMUS
INDEPENDENT LYMPHOSARCOMA
(0167)
- PREGNANCY
BREAST CANCER, LACTATION (0321)
HYDRAZINE, TOXICITY, RATS (0043)
- PROLACTIN
GROWTH OF MAMMARY TUMORS,
7,12-DIMETHYLBENZ(A)ANTHRACENE
(0927)
MAMMARY CARCINOGENESIS INHIBITION
(0440)
RAT MAMMARY GLAND, MITOTIC ACTIVITY
(1676)
RAT MAMMARY TUMOR, HYPOTHALAMIC LESION
(0770)
- PROLIFERATION
BONE MARROW, LEUKEMIA (2170)*
BONE MARROW, CHLORAMBUCIL, SERUM, RAT
(0901)
CELL KINETICS, NORMAL AND NEOPLASTIC
TISSUES, HUMAN LARYNGEAL TISSUES
(2051)
CELLULAR, ISOPROTERENOL, CYTOPLASMIC
RNA SYNTHESIS (0309)
CHICKEN EMBRYO CELLS, ROUS SARCOMA
VIRUS (1082)
CONTACT INHIBITION, CARCINOGENESIS
(1728)
CONTROL, LYMPHOCYTE, RECOGNITION SITE
(0008)
DNA SYNTHESIS, CELL DENSITY, EPITHE-
LIUM (0813)
FIBROBLASTIC, ACUTE MYELOFIBROSIS,
CHROMOSOME ABNORMALITY (1247)
FREUND'S ADJUVANT, GUINEA PIG, THYMUS
(1307)
GROWTH RATE, CANCER CELLS, METASTASES
GOMPERTZIAN CURVE (1732)
KINETICS, ACUTE LEUKEMIA, METHODS,
REVIEW (0876)*
KINETICS, CARCINOMA, 9,10-DIMETHYL-
1,2-BENZANTHRACENE, IRRADIATION
(0068)
KINETICS, DNA, SARCOMA -180 (1627)
KINETICS, MORRIS HEPATOMA (2050)
LYMPHOPROLIFERATIVE CHANGE, GERM-FREE
MICE (0168)
MELANIN SYNTHESIS, MOUSE PIGMENT CELL
(0812)
MITOTIC INDEX, NEUROBLASTOMA CELLS
(1242)
MOUSE KIDNEY CELLS, ISOPROTERENOL
(1674)
POPULATION DENSITY, NORMAL EMBRYO CELL
CULTURES, ROUS SARCOMA VIRUS,
POLYOMA VIRUS, SARCOMA 180 (0814)
ROUS SARCOMA VIRUS, CHICK EMBRYO CELL
(1083)
TUMOR GROWTH KINETICS, HUMAN LEUKEMIA
TUMOR CELLS (1281)
- PROPANE SULTONE
AZIRIDINE ETHANOL, SARCOMA INDUCTION
(1291)
CARINOGENICITY, PROPYLENE IMINE, RAT
(2263)
- BETA-PROIOLACTONE
TUMOR INDUCTION, HEPATOMA (0399)
- PROPYLENE IMINE
CARCINOGENICITY, PROPANE SULTONE, RAT
(2263)

STATE

BENIGN ADENOMA, NEOPLASTIC TRANSFORMATION, PREMALIGNANT CONDITION (0745)
BLUE NEVUS, MELANOCYTES (1239)
CANCER, HAMSTER, HUMAN, VIRUS, LACTATE DEHYDROGENASE ISOENZYMES (1508)
CARCINOMA, LACTATE DEHYDROGENASE, HAMSTER, HUMAN (2374)
CARCINOMA, SV40, PROGESTOGEN TREATMENT (1505)
CARCINOMA, TESTICLE, HUMAN (2572)
ESTROGEN, PROGESTERONE, DNA, RNA, RAT (0889)
HYPERPLASIA, ANDROGEN TREATMENT, PRAOMYS (MASTOMYS) NATALENSIS (0885)
VIRUS, VENEREAL DISEASE, CIRCUMCISION (2394)*

TEIN

ACCUMULATION, PHYTOHEMAGGLUTININ STIMULATION, HUMAN LYMPHOCYTE BLASTOGENESIS (0697)
ALBUMIN SYNTHESIS, MORRIS HEPATOMA, TOTAL PROTEIN SYNTHESIS (0305)
AMINOAZO DYE, 3'-METHYL-4-DIMETHYL-AMINOAZOBENZENE (0431)
BENCE JONES, IGA PARAPROTEINEMIA, BLAST CELL LEUKEMIA (0713)
BENZO(A)PYRENE, RNA, DNA, BINDING, METABOLISM (0941)
BINDING, COMPLEX FORMATION, CARBOHYDRATES, CARCINOGENESIS (0348)
BINDING, ORTHO-AMINOAZOTOLUENE, NUCLEIC ACID BINDING (0028)
CARCINOGEN BINDING, THE "DROP OUT" THEORY, REVIEW (0833)
CARCINOGEN BINDING IN RAT LIVER, 3-METHYLCHOLANTHRENE (1341)
COMPONENTS, AVIAN MYELOBLASTOSIS VIRUS (1064)
CONFORMATION, CELL GROWTH REGULATION, SERUM (1673)
ALPHA-FETOPROTEIN, AGE CORRELATION, LIVER (0231)
ALPHA-FETOPROTEIN, CARBOHYDRATE ANALYSIS, PROPERTIES (2002)
ALPHA-FETOPROTEIN, CARCINOEMBRYONIC ANTIGEN, GI CANCER (240)*
ALPHA-FETOPROTEIN, DIGESTIVE TRACT, TUMOR SPECIFIC ANTIGENS (0362)
ALPHA-FETOPROTEIN, ISOLATION, HEPATOMA, HUMAN (1580)*
ALPHA-FETOPROTEIN, LIVER, CARCINOMA (2003)
ALPHA-FETOPROTEIN, PRIMARY LIVER CANCER, LOCALIZATION, HUMAN (2004)
GAMMA1-IMMUNOGLOBULIN, HEAVY CHAIN, PRIMARY STRUCTURE, MYELOMA (1581)*
GLYCOPROTEIN, MAMMARY TUMOR AGENT, ANTIGEN (0191)
GLYCOPROTEIN COMPONENT, ROUS SARCOMA VIRUS, AVIAN TUMOR VIRUS (0202)
GLYCOPROTEIN SYNTHESIS, POLYOMA VIRUS, HAMSTER KIDNEY (1114)
GROUP-SPECIFIC, CANCER PATIENTS (1569)
HAPTOGLOBIN TYPES, LEUKEMIA PATIENTS (2023)*
HEPATOMA HISTONE, N-ACETYLTATION, NORMAL AND NEOPLASTIC RAT LIVER (2056)

INTRAMOLECULAR MODIFICATION, KINETICS, CARCINOGENS, ROLE IN TRANSFORMATION PROCESSES (1162)

LAMBDA, MYELOMA, SERUM (1127)

METABOLISM, LABELED METHIONINE INCORPORATION, MAMMARY GLAND TUMOR, MOUSE (0793)

MUCOPROTEIN, URINE OF CANCER PATIENTS, ANEMIA-INDUCING PLACENTAL SUBSTANCE, COMMON ANTIGENICITY (1575)

MYELOMA, HEAVY CHAIN MUTANTS, MOUSE (1564)

PARAPROTEIN, A-TYPE VIRUS-LIKE PARTICLES, MURINE PLASMA CELL NEOPLASIA (0593)

PARAPROTEIN, ELECTROPHORESIS, MULTIPLE MYELOMA (0333)*

PARTICULATE THYROID PROTEINS, TUMOR (0255)

PLASMA, IRRADIATION, RATS, ESTERASE ACTIVITY (1387)

PRINCIPAL PROTEIN CONJUGATES, CHEMICAL HEPATOCARCINOGENS (0050)

RAT LIVER H, ANTI-H, 3'-METHYLDIAZOBENZENE (0053)

RIBONUCLEOPROTEIN SYNTHESIS, MITOCHONDRIA, HELA CELL (2570)

RIBOSOMAL, SYNTHESIS, EHRLICH'S TUMOR (2529)

ROUS SARCOMA VIRUS, STRUCTURAL (1482)

S100, BRAIN GLIOMAS (1567)

SERUM PARAPROTEIN, PLASMACYTOMA CELLS (0729)

STRUCTURAL, ADENOVIRUS 2 (1912)

STRUCTURAL, ADENOVIRUS TYPE 2 VIRION, DEGRADATION PRODUCTS (0613)

STRUCTURAL, HERPES SIMPLEX VIRUS (1462)

STRUCTURAL, SV40, KIDNEY (1953)

STRUCTURAL VIRAL PROTEINS, KILHAM RAT VIRUS (1071)

STRUCTURE, PLASMACYTOMA, MYELOMA, MOUSE (2006)

SULFHYDRYL GROUPS, ENDOMETRIUM, ADENOCARCINOMA, HUMAN (2468)

SURFACE ANTIGENS, AVIAN TUMOR VIRUSES (1085)

SYNTHESIS, ADENOVIRUS 2, METHIONINE INITIATION (1911)

SYNTHESIS, ECTOPIC HORMONE PRODUCTION BY MALIGNANT CELLS, POLYPEPTIDE HORMONE PRODUCTION, REVIEW (0832)

SYNTHESIS, FRIEND VIRUS, INFECTED SPLEEN CELLS (1032)

SYNTHESIS, LIVER, CARCINOGENS (2151)

SYNTHESIS, MYELOMA CELL-LYMPHOMA CELL HYBRID, ANTIGEN (1124)

SYNTHESIS, NUCLEIC ACIDS, PAPOVA VIRUS (1426)

TRANSFER OF PROTEINS TO NUCLEOLUS, MOUSE ASCITES TUMOR (1658)

VIRUS, ADENOVIRUS 5, ARGININE, HUMAN CELLS (2328)

PSEUDOVIRUS

DNA, MOUSE EMBRYO CELLS, POLYOMA (0683)

SIMIAN, MOUSE EMBRYO CELLS, DNA (1094)

PUBERTY
 GROWTH PEAK, BONE CANCER (0314)
 12H-PYRIDO(2,3-A)THIENO(2,3-I)-
 CARBAZOLE
 STRUCTURE-ACTIVITY RELATIONSHIP, MOUSE
 (0411)
 PYRROLIZIDINE ALKALOID
 PANCREATIC ISLET CELL TUMOR, AMSINCKIA
 INTERMEDIA FISCH, HELIOTROPICUM
 SUPINUM (0033)
 4-QUINOLINE-1-OXIDE
 TERTIARY BUTYL HYDROPEROXIDE, FREE
 RADICAL, SQUAMOUS CELL CARCINOMA,
 MICE (0026)
 RADIATION
 ACUTE, THYMECTOMY, HEMATOPOIESIS, MICE
 (1001)
 ADENOCARCINOMA, GIANT RENAL CYST
 (1861)*
 ALPHA PARTICLE IRRADIATION, FIBRO-
 SARCOMA, RAT (0992)
 ALPHA2-GLOBULIN, BLOOD, BONE MARROW,
 CELL POPULATION (2278)
 AMERICUM 241, HISTOLOGICAL DISTRIBUTION
 IN RAT, PATHOGENESIS (1016)*
 ATOMIC BOMB, BENZENE, OCCUPATIONAL
 EXPOSURE, LEUKEMIA INCIDENCE (1399)
 ATOMIC BOMB IRRADIATION, CHILDHOOD
 CANCER INCIDENCE, CANCER MORTALITY
 (0540)
 ATOMIC BOMB SURVIVORS, JAPAN,
 INCIDENCE OF LEUKEMIA (1398)
 BETA-RADIATION, EXPERIMENTAL OSTEO-
 SARCOMA, FEMORAL METAPHYSIS, RAT
 (0543)
 BLOOD, DNA SYNTHESIS, LYMPHOCYTES,
 PHYTOHEMAGGLUTININ (0526)
 BOMB IRRADIATION, TUMORIGENESIS, SWINE
 (0994)
 BONE MARROW, ALPHA2-GLOBULIN, MOUSE
 (2276)
 BONE MARROW LYMPHOCYTES, SPLENIC
 LYMPHOCYTES, CYTOMETRIC STUDY (0534)
 BURN SCARS, BASAL CELL CARCINOMA (0531)
 CARCINOMA, CERVICAL, RECTAL (1395)
 CELL DEATH, MITOTIC BLOCK, PHYTO-
 HEMAGGLUTININ (1136)
 CERIUM 144, TISSUE DISTRIBUTION IN
 DOGS, ONCOGENICITY (1015)
 CHRONIC, ECCRINE POROMA, THUMB (0134)
 COBALT 60, GAMMA IRRADIATION, LYSOZYME
 ENZYME (2292)
 COBALT 60, METAPHASE CHROMOSOME
 ABERRATIONS, HAMSTER LIVER CELLS
 (1394)
 COBALT 60, 3H-URIDINE IRRADIATION,
 CHROMOSOME ABERRATIONS (0521)
 EPIDERMAL CHANGES, 10B(N,ALPHA)7LI
 REACTION, SWINE (1384)
 EXPOSURE, HYPOPHARYNX, CARCINOMA
 (0995)
 FACE AND LIP, MELANOMA (0547)
 FEMUR, 90S GAMMA, 90Y, DOSIMETRY, RAT
 (1405)*
 FISSION NEUTRON IRRADIATION, ADRENAL
 CARCINOMAS (0532)
 FRIEND LEUKEMIA VIRUS, HEMATOPOIESIS
 (1898)

GAMETES, ZYGOTES, DROSOPHILA MELANO-
 GASTER, CARCINOGENESIS (0998)
 GAMMA-IRRADIATION, 7,12-DIMETHYL-
 BENZ(A)ANTHRACENE, URETHAN, HORMON
 (1789)
 GAMMA-IRRADIATION, MOUSE DUODENAL
 EPITHELIUM, CELL PRODUCTION (0123)
 CO 60-GAMMA IRRADIATION, BRONCHIAL
 EPITHELIUM, DRY WEIGHT AND HYDRATION
 CHANGES (1850)
 GAMMA-RADIATION, RETINA, DYSPLASIA,
 DOG (0525)
 GAMMA RAY, FROG VIRUS 3, DNA
 REPLICATION (0522)
 GAMMA RAY, INTESTINAL CAPILLARIES,
 FRACTIONATED DOSE (1383)
 GAMMA RAY, RAT LIVER, ALPHA-AMINO-
 ISOBUTYRIC ACID (1386)
 HEAVY ION IRRADIATION, MUTAGENESIS,
 ARABIDOPSIS PLANT (0539)
 HEMATOPOIESIS, MOUSE (2277)
 HEMATOPOIETIC REGENERATION, TESTO-
 STERONE (1848)
 HEPATOMA, N,N'-2,7-FLUORENYLENEBIS-
 ACETAMIDE, ACCELERATED INDUCTION
 (0040)
 IMMUNITY, MAMMARY CARCINOMA, MICE
 (2416)
 INJURY, BONE MARROW TRANSPLANTATION,
 SPLENECTOMY (0533)
 INTESTINE, CELL DEPLETION KINETICS,
 MOUSE (2282)
 IONIZING, HUMAN BONE MARROW (0993)
 IONIZING IRRADIATION, PULMONARY
 ISCHEMIA (0124)
 ISOLATED LIVER, AMINO ACIDS, PERFUSION,
 ACTIVE TRANSPORT (0537)
 LECITHIN METABOLISM IN LUNG, SURFACE
 ACTIVITY OF LUNG (0542)
 LEUKEMIA, BONE MARROW AUTOTRANSPLANTATION,
 MOUSE (1864)*
 LEUKEMIA, THERAPEUTIC DOSE, MALIGNANT
 (0370)
 LEUKEMOGENESIS, 7,12-DIMETHYLBENZ(A)
 ANTHRACENE, BONE MARROW CELLS
 (0928)
 LEUKEMOGENESIS, VIRUS, HOST FACTORS,
 MICE (2434)
 LYMPHOCYTE, CHROMOSOME, ABERRATION,
 HUMAN (1008)
 LYMPHOMA, INACTIVATION, IMMUNOLOGY,
 MOUSE (0223)
 MANDIBULAR FIBROUS DYSPLASIA,
 OSTEOGENIC SARCOMA (1408)*
 NEUTRON, GAMMA RAY, HEMOPOIETIC CFU
 (1380)
 NEUTRON, MOUSE EPIDERMAL CELLS, CELL
 SURVIVAL (1409)*
 NEUTRON IRRADIATION, PIG LEUKOCYTES,
 CHROMOSOME ABERRATIONS (1005)
 NUCLEAR BOMB, GASTRIC CARCINOMA (111)
 ORAL CAVITY, VERROUS EPIDERMAL
 CARCINOMA, ANAPLASTIC TRANSFORMATION,
 HUMAN (0131)
 OSTEOSARCOMA, STRONTIUM 90, RAT
 (1410)*
 OVARY, CHORIONIC GONADOTROPIN, TUMOR
 DEVELOPMENT (1594)

PHILADELPHIA CHROMOSOME, ACUTE
 LYMPHOCYTIC LEUKEMIA (0130)
 32 PHOSPHORUS, ULTRASTRUCTURE, OSTEO-
 SARCOMA (0548)
 PLUTONIUM, RETENTION IN BONE CELLS
 (1012)
 PLUTONIUM AEROSOL, RAT LUNG ALVEOLI
 (1843)
 POSTIRRADIATION SARCOMA (0132)
 POTENTIATION OF TUMORIGENICITY,
 PASSAGE IN VITRO OF SV40 (1093)
 PROTEIN-BOUND NEUTRAL HEXOSES, HYPATO-
 CYTIC ULTRASTRUCTURAL CHANGES (0546)
 PROTON-IRRADIATION, DEEP BRAIN LESION,
 HISTOPATHOLOGY (1007)
 QUARTZ, SILICOSIS, PLEURAL MESO-
 THELIOMA (0996)
 RADIOACTIVE IODINE, THYROTOXICOSIS,
 IATROGENIC CANCER (0549)
 RADIONUCLIDES, LEUKEMIA, SARCOMA,
 REVIEW (1274)
 RADIUM EXPOSURE, CHILDREN, BONE CANCER
 INDUCTION (1000)
 RADIUM 224, OSTEOBLASTIC SARCOMA,
 ALKALINE PHOSPHATASE, MICE (1382)
 RARE EARTH METALS, 7,12-DIMETHYLBENZ-
 (A)ANTHRACENE, 1,2,5,6-DIBENZANTHRA-
 CENE, RAT (2294)*
 RATS, ESTERASE, PLASMA (1387)
 RETROMANDIBULAR DAMAGE, THOROTRASTOMA
 (1862)*
 SARCOMA, SCAPULA, AXILLA, HUMAN (0133)
 SEX CHROMATIN, ENDOMETRIAL CANCER
 (0810)
 SIMIAN VIRUS 40, MICE (0211)
 SKIN, HEMANGIOMA, CASE REPORT (1401)*
 SKIN, LIGHT, LIPID METABOLISM (1856)
 SKIN, NEUTRON BEAM, SWINE (1385)
 STRONTIUM, HAEMATOPOIESIS, SPLEEN,
 THYMUS, BONE MARROW (1379)
 STRONTIUM 90, ADENOVIRUS (1838)
 STRONTIUM 90, INHALATION OF 90SR BY
 DOGS, CARCINOGENICITY (1014)
 STRONTIUM 90, IODINE 131, RESPIRATORY
 PATTERN, MOUSE (2284)
 STRONTIUM 90, LEUKEMIA, MOUSE (2285)
 STRONTIUM 90, MYELOID NEOPLASMS IN
 SWINE, LEUKEMIA (1841)
 STRONTIUM 90, OSTEOSARCOMA, BONE
 MARROW (1381)
 STRONTIUM 90, RETENTION IN ORGANS,
 BEAGLE DOGS (1013)
 SUNLIGHT, MALIGNANT MELANOMA (0835)
 SUNLIGHT, MELANOMA, SOLAR CIRCULATING
 FACTOR (0861)
 SUNLIGHT, SQUAMOUS CELL CARCINOMA,
 CAT (2288)
 SUNLIGHT, SQUAMOUS CELL CARCINOMA OF
 SKIN, HAND AND ARM (0997)
 SUNLIGHT EXPOSURE, HUMAN EPIDERMIS,
 ULTRASTRUCTURAL STUDY (1855)
 SUPRA-LETHAL DOSE, CHANGES IN LUNG
 TISSUE (1009)
 THERAPY, RADIATION-INDUCED THYROID
 NEOPLASMS, NODULAR GOITERS (0138)*
 THORIUM 232, CIGARETTE SMOKERS,
 ACCUMULATION OF THORIUM IN LUNGS
 (1400)
 THORIUM 232, HUMAN BONE (1006)
 THOROTRAST, HUMAN LIVER, CIRRHOSIS,
 CARCINOMA (1397)
 THOROTRAST, 131I-LIPIODOL (0845)
 THOROTRAST, TUMORS, LIVER, KIDNEYS
 (0366)
 THYMUS TUMORS, CHILDHOOD (1396)
 TRANSFORMATION, IN VITRO, REVIEW
 (0390)*
 TRANSPLANTATION, LUNG, ADENOMA, MOUSE
 (2286)
 TUMORIGENESIS, OVARY, MOUSE (1845)
 TUMORIGENESIS, RISK, RADIUM (0836)
 239PU EXPOSURE, RISK OF TUMOR DEVELOP-
 MENT (1003)
 ULTRAVIOLET, FIBROBLASTS, HAMSTER
 (1851)
 ULTRAVIOLET, FIBROBLASTS, XERODERMA
 PIGMENTOSUM (1388)
 ULTRAVIOLET, MURINE LEUKEMIA VIRUS,
 MURINE SARCOMA VIRUS, INACTIVATION
 (1452)
 ULTRAVIOLET, T ANTIGEN, SV40, ADENO-
 VIRUS 12 (1978)
 ULTRAVIOLET, VIRUS, BRAIN (1489)
 ULTRAVIOLET INACTIVATION, ROUS SARCOMA
 VIRUS HELPER (1479)
 ULTRAVIOLET IRRADIATION, MURINE SAR-
 COMA VIRUS INFECTION, CELL CYCLE
 (0198)
 UTERUS, CARCINOGENICITY, RAT (1846)
 UV, BENZ(A)PYRENE, DNA, PHOTO ADDUCT
 (0938)
 UV, PHOTOCHEMICAL LESION, MOUSE (0536)
 UV IRRADIATION, ENHANCEMENT OF VIRAL
 TRANSFORMATION (0663)
 UV IRRADIATION, NON-PROLIFERATING
 ACUTE LEUKEMIA CELLS, DNA SYNTHESIS
 (1223)
 UV IRRADIATION, SV40, SURVIVAL (0668)
 UV IRRADIATION, TRANSFORMING CAPACITY,
 AVIAN SARCOMA VIRUS (0640)
 UV LIGHT, CROTON OIL, ACETIC ACID,
 XYLENE, MOUSE (0545)
 VISIBLE LIGHT, AVIAN SARCOMA VIRUS,
 5-BROMOURIDINE, CHICK EMBRYO FIBRO-
 BLAST (0641)
 WHOLE BODY, ADRENAL GLAND, HISTO-
 CHEMISTRY, RAT (1407)*
 WHOLE BODY IRRADIATION, LUNG HISTO-
 CHEMISTRY, RAT (0127)
 WHOLE BODY IRRADIATION, LUNG ULTRA-
 STRUCTURE, ACID AND ALKALINE PHOS-
 PHATASE, GLYCINE INCORPORATION, RAT
 (0128)
 WHOLE BODY IRRADIATION, SKIN LESIONS,
 HISTAMINE, BLOOD, RAT (0139)*
 WHOLE BODY IRRADIATION, SPLEEN
 LEUKEMOGENIC VIRUS, MOUSE (0592)
 X-IRRADIATION, ATOMIC BOMB SURVIVORS
 (1854)
 X-IRRADIATION, CHROMOSOME ABERRATIONS,
 RABBIT, HUMAN (2280)
 X-IRRADIATION, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, SKIN PAPILLOMA, MOUSE
 (2219)
 X-IRRADIATION, FIBROSARCOMA INDUCTION,
 HUMAN (1849)

X-IRRADIATION, GROSS LEUKEMIA VIRUS, LEUKEMOGENESIS, SYNERGISM (0604)
 X-IRRADIATION, HORMONES, LIVER, POLYRIBOSOMES (0544)
 X-IRRADIATION, IODINE 131, THYROID, CHROMOSOME DAMAGE, HUMAN (2283)
 X-IRRADIATION, LEUKEMIA INDUCTION, STRONTIUM 90 (1639)
 X-IRRADIATION, LIVER, KIDNEY, MOUSE (2279)
 X-IRRADIATION, LYMPHOMA, RESISTANCE, MOUSE (2289)
 X-IRRADIATION, MAMMARY NEOPLASIA, IRRADIATED GRAFT (1847)
 X-IRRADIATION, METHIONINE SULFOXIMINE, BONE MARROW CELL COUNTS (0405)
 X-IRRADIATION, MITOTIC DELAY, CHROMOSOMAL ABERRATION, CYSTEAMINE (0129)
 X-IRRADIATION, MOUSE LEUKEMIA CELLS, ALLOGRAFT SURVIVAL (0225)
 X-IRRADIATION, MURINE LYMPHOMA CELLS, DOUBLE-STRAND DNA BREAKS (0523)
 X-IRRADIATION, MYXOVIRUS INFECTION, CHROMOSOME ABERRATIONS (1002)
 X-IRRADIATION, NUCLEIC ACID SYNTHESIS, HAMSTER CELLS (2290)
 X-IRRADIATION, NUCLEOLAR MORPHOLOGY, THYMIC LYMPHOCYTES (1842)
 X-IRRADIATION, PYRUVATE, THYMOCYTES, RAT (2293)
 X-IRRADIATION, RAT BONE MARROW, MITOTIC ABERRATIONS (1844)
 X-IRRADIATION, SPERMATOZOA, DOMINANT LETHALITY, MOUSE, RAT (2281)
 X-IRRADIATION, SPLEEN, BONE MARROW, REGENERATION, MOUSE (2275)
 X-IRRADIATION, SPLEEN IMMUNE RESPONSE, BURSECTOMY (1134)
 X-IRRADIATION, SPONTANEOUS LYMPHOMAS, VIRUS PARTICLES, HAMSTER (1868)
 X-IRRADIATION, STEM CELL PROLIFERATION, BONE MARROW STEM CELLS (1011)
 X-IRRADIATION, STRONTIUM 90, LEUKEMIA INDUCTION (1839)
 X-IRRADIATION, ULTRAVIOLET, ACID PHOSPHATASE, MOUSE ENDOCRINE GLANDS (2287)
 X-IRRADIATION, WHOLE BODY, PROTEASE ACTIVITY, RABBIT (2274)
 X-IRRADIATION IN UTERO, CHROMOSOME ABERRATIONS (0538)
 X-RAY AND NEUTRON IRRADIATION, CELL SURVIVAL AND REPAIR, JEJUNAL MUCOSAL CRYPT CELLS (0524)
 X-RAY, CHEMICAL CARCINOGENS, VIRUS PRODUCTION BY INFECTED CELLS (1424)
 X-RAY, DNA SYNTHESIS, KIDNEY, EHRlich CELLS, LIVER (1390)
 X-RAY, DNA SYNTHESIS, NEUROBLASTS (1391)
 X-RAY, ESTROGEN TREATMENT, MAMMARY CARCINOGENESIS (1295)
 X-RAY, FORWARD MUTATIONS, 8-AZAGUANINE SENSITIVITY (1393)
 X-RAY, LEUKEMIA, CHILDHOOD CANCER (1605)

X-RAY, LEUKEMIA, HYDROCORTISONE, MICE (0999)
 X-RAY, LYMPHOID CELLS, IMMUNOLOGIC COMPETENCE (1544)
 X-RAY, TRANSLOCATION INDUCTION, MOUSE SPERMATOGENIA (1392)
 X-RAY THERAPY, STOMACH CANCER, FIBROSIS (0136)
 RADIOACTIVITY
 FALLOUT, RADIOACTIVE IODINE, THYROID NEOPLASIA (0529)
 RADIOIODINE 131
 THYROID, FOLLICULAR ATROPHY, RAT (0125)
 RADIUM
 KINETICS, BONE MARROW-FREE SKELETON THOROTRAST, MODEL, RABBIT (1403)*
 POISONING, LYMPHOMYELOID CARCINOMA, OSTEOSARCOMA (0001)
 REGENERATION
 LIVER, MOUSE HEPATOMAS, URETHAN (0999)
 X-IRRADIATION, SPLEEN, THYMUS, BONE MARROW, MOUSE (2275)
 RESCUE
 PSEUDOTYPE SARCOMA, MURINE LEUKEMIA VIRUS, NEW ZEALAND BLACK MICE (0606)
 RESERPINE
 7,12-DIMETHYLBENZ(A)ANTHRACENE, MAMMARY TUMOR (0929)
 RESISTANCE
 FRIEND VIRUS, LEUKEMIA, REGRESSION, MOUSE (2412)
 SV 40, GREEN MONKEY KIDNEY CELLS (0214)
 TUMOR, TRANSFER, METHYLCHOLANTHRENE RAT SARCOMA (1983)
 RESPIRATORY TRACT
 CANCER, COKE WORKERS, STEELWORKERS, MORTALITY RATES (1369)
 CARCINOMA OF THE TONSIL, URBAN AIR POLLUTION, CANINE (1183)
 CIGARETTE SMOKE, HAMSTERS, SMOKE PARTICLE DEPOSIT, LUNGS (1366)
 N-NITROSO-N-METHYLUREA, EPIDERMAL CARCINOMA, HAMSTER (0482)
 RETICULOENDOTHELIAL SYSTEM
 THOROTRAST, 131I-LIPIODOL, REVIEW (0845)
 RETICULOENDOTHELIOSIS VIRUS
 LEUKEMIC, ACID PHOSPHATASE ISOENZYME, RETICULUM CELLS (1637)
 MAREK'S DISEASE, PERIPHERAL NERVE LESIONS (0161)
 RETICULOPROLIFERATIVE DISEASE
 HERPESVIRUS SAIMIRI, VIRUS, RINGTAIL CINNAMON MONKEY (1059)
 RETICULOSARCOMA
 CELL LINES IN HEMATOPOIETIC TISSUES, CYTOLOGIC STUDY (1224)
 LYMPHOID, HISTIOCYTIC SARCOMA, HISTIOBLASTIC SARCOMA, ULTRASTRUCTURE (2108)
 RETINA
 DYSPLASIA, RADIATION, DOG (0525)
 RETINOBLASTOMA
 BLOOD, MALIGNANT CELLS (1666)
 CHROMOSOMAL ABERRATIONS, KARYOTYPE ANALYSIS (0805)

DEVELOPMENTAL ABNORMALITIES, DQ-- AND
DR-- CHROMOSOME CONDITIONS (0806)
IN VITRO CULTURE, MALIGNANT TRANS-
FORMATION (1234)
RDOMYOSARCOMA
ANTIGENS, IMMUNITY, MOUSE (1987)
CHROMOSOME, DOUBLE-MINUTE, HUMAN (2525)
DNA REPLICATION, HUMAN (1230)
EPIDERMODYSPLASIA VERRUCIFORMIS,
VIRUS-LIKE PARTICLES (1017)
AMINE
SARCOMA, GLUCOSE-6-PHOSPHATE
DEHYDROGENASE ISOZYMES, LIVER, RAT
(0035)
OFLAVIN
DEFICIENCY, 7,12-DIMETHYLBENZ(A)-
ANTHRACENE, SKIN TUMORS (0935)
OSOME
MITOCHONDRIA, HELA CELLS (2528)
ANTIBIOTICS, EXORIBONUCLEASE, EHRLICH
ASCITES TUMOR (2179)
ARGINYL-TRNA, SERYL-TRNA, HUMAN
EPIDERMOID CARCINOMA, HERPES SIMPLEX
(1058)
AVIAN LEUKOSIS, VIRUS (1887)
AVIAN SARCOMA VIRUS, NONTRANSFORMANT
(1066)
BENZ(A)PYRENE, IMMUNOREACTIVITY,
TRANSFER (0222)
BENZ(A)PYRENE, TUMOR IMMUNITY TRANSFER
(0728)
BONE, SARCOMA GROWTH, RAT (0817)
CARCINOMA, EARLY STAGE, MUCOSA,
HISTOLOGY (1599)*
CARCINOMA, HEREDITARY DISTRIBUTION,
FAMILIAL POLYPOSIS OF THE COLON
(1245)
CARCINOMA, MUCOSAL FOLDS (1592)
CARCINOMA, RADIATION THERAPY, CERVICAL
CARCINOMA (1395)
CHROMATIN, LIVER, HEPATOMA, RAT (2198)
CHRONIC LYMPHOCYTIC LEUKEMIA, HUMAN
(2517)
CYTOPLASMIC SYNTHESIS, CELL PROLIFERA-
TION, ISOPROTERENOL (0309)
DNA, NUCLEIC ACID METHYLASES (2150)
DOUBLE STRANDED PENICILLIUM, REGRESS-
ION OF SPLENOMEGALY, VIRUS, FRIEND
LEUKEMIA VIRUS (1450)
FELINE LEUKEMIA VIRUS (1440)
HARDING-PASSEY CELLS, MELANOMA,
MUSCLE, RAT LIVER (2077)
HISTONES, INHIBITION, LEUKEMIA, HUMAN
(2515)
N-HYDROXY-ACETYLYAMINOFLUORENE,
POLYRIBONUCLEOTIDE BINDING (0406)
KIDNEY, AFLATOXIN B1, MOUSE (2207)
LEUKEMIA, DNA POLYMERASE (0792)
LIVER, HEPATOMA, RAT (2546)
LIVER, HEPATOMAS, SUBRIBSOMAL
PARTICLES (1636)
LIVER NULCEAR, POLYMERASE, AFLATOXIN
B1, RAT (0046)
LOW MOLECULAR WEIGHT, 4S, ROUS SARCOMA
VIRUS (0646)
LYSYL-TRANSFER, DIETHYLSTILBESTEROL,
CHICKEN LIVER (1205)

MESSANGER, FREE, POLYRIBOSOME BOUND,
HELA CELLS (1203)
MESSANGER, SARCOMA 180 ASCITES,
POLYSOME (2071)
METABOLISM, THIOACETAMIDE, RAT LIVER
(1775)
METABOLISM, AMINE SYNTHESIS, THIO-
ACETAMIDE (0039)
METHYLATING ENZYMES, VIRUS, E.COLI
(2304)
METHYLATION, DIMETHYLNITROSAMINE,
S-ADENOSYL METHIONINE, RAT LIVER
(0082)
MILK, DNA POLYMERASE, HUMAN (1878)
M-RNA, SENDAI VIRUS, HAMSTER, CHICK
EMBRYO (0207)
M-RNA SYNTHESIS, POLYOMA VIRUS,
MOUSE EMBRYO CELLS (0218)
MURINE SARCOMA, VIRUS SPECIFIC (2355)
MURINE SARCOMA-LEUKEMIA, VIRUS
(1076)
MURINE VIRUSES, HOST RANGE ALTERATION,
HUMAN CELL CULTURES (2352)
MYELOBLASTOSIS, BAI AVIAN LEUKOSIS
VIRUS (1890)
NEOPLASTIC TISSUE, GROWTH AND DIFFER-
ENTIATION, TRANSFER RNA METHYLASE
ACTIVITY (0791)
NORMAL TISSUE, MURINE LEUKEMIA
TRANSPLANT, IMMUNOSUPPRESSION (1557)
NUCLEAR, AFLATOXIN, HEPATOCYTES, RATS
(1780)
NUCLEAR, MAMMARY CELLS, NEOPLASTIC,
MOUSE (2062)
NUCLEAR SYNTHESIS, FRIEND VIRUS (0601)
NUCLEOTIDE COMPOSITION, HYBRIDIZATION,
VIRUS (1942)
PHENYLALANINE TRANSFER, LEUKEMIA,
LYMPHOMA, HUMAN (2520)
PHENYLALANINE TRANSFER SYNTHETASE,
(2521)
POLYINOSINIC ACID/POLYCYTIDYLIC ACID
RNA, SKIN TUMOR, 7,12-DIMETHYLBENZ-
(A)ANTHRACENE, MOUSE (0447)
POLYMERASE, MAMMALIAN, VIRUS, DNA
(1103)
RAUSCHER MURINE LEUKEMIA VIRUS,
NUCLEOCAPSID (0176)
RIBOSOMAL, FIBROBLASTS, ACTINOMYCIN D
(1659)
RIBOSOMAL TRANSFER, BRAIN TUMORS,
HUMAN (2087)
SARCOMA, BENZOPYRENE, IMMUNITY, RAT
(2428)
SARCOMA, ISOGRAFTS, MURINE (1988)
SARCOMA, ROUS VIRUS, CHICKEN, MOUSE
(2365)
SELF-REPLICATING, LEUKEMIA, VIRUS
(0572)
SERYL TRNA, ESTROGEN, PHOSVITIN,
ROOSTER (2475)
7S, ROUS SARCOMA VIRUS (1088)
SPLEEN, RAUSCHER VIRUS, MOUSE (1038)
SYNTHESIS, ACETAMIDOFLUORENE
DERIVATIVES, RADIOACTIVE PRECURSOR
INCORPORATION (0408)
SYNTHESIS, AFLATOXIN B1, HEPATECTOMY,
LIVER, RAT (2205)

SYNTHESIS, BROMODEOXYURIDINE, ROUS SARCOMA VIRUS (0645)
 SYNTHESIS, HUMAN LYMPHOCYTE AGGREGATE ENZYME, PHYTOHEMAGGLUTININ (1138)
 SYNTHESIS, INFECTION, ADENOVIRUS 12, HAMSTER (2329)
 SYNTHESIS, LIVER CELLS, AFLATOXIN B1 (0914)
 SYNTHESIS, 3-METHYLCHOLANTHRENE, CHROMATIN, RAT LIVER NUCLEI (0463)
 SYNTHESIS, POLYOMA VIRUS, MOUSE (2400)*
 SYNTHESIS, TOYOCAMYCIN, VIRUS-INFECTED CHICK EMBRYO CELLS (1105)
 SYNTHESIS INHIBITION, HUMAN KIDNEY CELLS, H-1 VIRUS, VIRUS (1099)
 TRANSCRIPTASE ACTIVITY, VIRUS, WOUND TUMOR VIRUS (0148)
 TRANSFER, N-ACETOXY-2-ACETYLAMINO-FLUORENE (2199)
 TRANSFER, BRAIN TUMOR, BASE COMPOSITION (2527)
 TRANSFER, ESCHERICHIA COLI, 5-METHYLURIDINE (2508)
 TRANSFER, ESCHERICHIA COLI, MUTATION (2148)
 TRANSFER, HYPERMETHYLATION, DIMETHYL SULFATE (0319)
 TRANSFER, ISOACCEPTING, RETICULOCYTES, PLASMA CELL TUMORS, MICE (2504)
 TRANSFER, LEUKEMIA, EMBRYONIC TISSUE (2503)
 TRANSFER, LEUKEMIA, LYMPHOBLAST (1204)
 TRANSFER, LEUKEMIC LYMPHOBLASTS, AMINOACYLATION (0790)
 TRANSFER, LIVER, MORRIS 5123 HEPATOMA (2025)
 TRANSFER, MAMMALIAN TISSUE, SPECIFICITY (2505)
 TRANSFER, METHYLASE, BRAIN TUMORS, HUMAN (2523)
 TRANSFER, METHYLASE, CONTROL (2511)
 TRANSFER, METHYLASE, MORRIS HEPATOMA (2512)
 TRANSFER, METHYLASES, REVIEW (0831)
 TRANSFER, METHYLATION, ASCITES TUMOR, MOUSE (2509)
 TRANSFER, METHYLATION, MAREK'S DISEASE VIRUS (2309)
 TRANSFER, METHYLATION, NEOPLASIA, MICE (1200)
 TRANSFER, METHYLATION, NEOPLASIA, REVIEW (2147)
 TRANSFER, METHYLATION, NEOPLASTIC CELLS (2507)
 TRANSFER, MODIFIED BASES, E. COLI (2518)
 TRANSFER, MORRIS HEPATOMAS, ALTERATIONS, RAT (2090)
 TRANSFER, MORRIS HEPATOMA, LIVER, OVA (2526)
 TRANSFER, PHENYLALANINE, HEPATOMA, MOUSE (2585)*
 TRANSFER, POLYOMA VIRUS, METHYLATION (0217)
 TRANSFER, POLYOMA VIRUS, RAT (1962)
 TRANSFER, SYNTHESIS, BACTERIOPHAGE, E. COLI (2513)
 TRANSFORMED CELLS, AVIAN MYELOBLASTOSIS VIRUS, CHICKEN (1026)
 TRNA GUANINE 7-METHYLASE, MAMMARY TUMOR, MOUSE (2506)
 TUMOR, IMMUNITY, GUINEA PIG (2464)*
 TUMOR-IMMUNIZED ANIMALS, ENHANCEMENT OF TUMOR ISOGRAFT (1561)
 VILLOUS ADENOMA, ELECTROLYTE DISTURBANCE, POTASSIUM LOSS (1211)
 VIRAL, HYBRIDIZATION, DNA-POLYMERASE CHICK LEUKEMIC VIRUS, BASE SEQUENCE (1438)
 VIRAL RNA--DNA HYBRID MOLECULE, DNA POLYMERASE TEMPLATE, SARCOMA-LEUKEMIA (0143)
 VIRION RNA SYNTHESIS (1940)
 VIRUS, MAMMARY TUMORS (1927)
 VIRUS, MURINE MAMMARY TUMOR, FLUORESCENCE MICROSCOPY (1469)
 VIRUS-SPECIFIC, ROUS SARCOMA (1487)
 YEAST, TUMOR SURVIVAL TIME, IMMUNIZED MICE (1556)
 SALIVARY GLAND
 GARDNER'S SYNDROME (1601)*
 MALIGNOMA, POLYMORPHIC ADENOMA, EPIDEMIOLOGY, EASTERN GERMANY (028)
 MIXED TUMOR, HUMAN (0251)
 NEOPLASM, ENVIRONMENT, VITAMIN A, 7,12-DIMETHYLBENZANTHRACENE, RAT (0308)
 TUMOR, MYOEPIHELIAL CELL (2163)
 TUMOR, POLYOMA VIRUS (0219)
 SARCOMA
 ADENOVIRUS TYPE 12, IMMUNOLOGY, HAMSTER (0618)
 ANTIBODY, HUMAN, VIRUS (0147)
 ASCITIC, 3-METHYLCHOLANTHRENE, CYTOGENETICS, HAMSTER (1219)
 ASCITIC TUMOR, ROUS SARCOMA VIRUS, NUCLEIC ACID, MOUSE CELL (1080)
 AVIAN LEUKOSIS, PATHOLOGY, MORPHOLOGICAL PARTICLES (0324)
 AXILLARY REGION, 3,4-BENZOPYRENE, MOUSE (0467)
 BLOCKADE, ROUS SARCOMA VIRUS, RABIES VIRUS VACCINE, CHICKEN (0652)
 DEFECTIVE MOLONEY VIRUS, MAZURENKO VIRUS, MOUSE (1475)
 FERRIDEXTRAN SPOFA, ANTIGENICITY, RAT (0900)
 GROWTH, BONE MARROW, RAT (0817)
 HERPES VIRUS HOMINIS, HAMSTER (0185)
 K-237, SKIN-HETEROGENIZING VIRUS, MICE (0144)
 LEIOMYOSARCOMA, N-METHYL-N'-NITRO-NITROSOGUANIDINE, MOUSE GASTRIC CYST (1354)
 LEUKEMIA, RADIONUCLIDES, REVIEW (127)
 MCG1-SS, MCG1-AS, 20-METHYLCHOLANTHRENE, METASTASIS (0078)
 MELANOMA, IMMUNOCOMPETENCE, IMMUNOTHERAPY, HUMAN (0704)
 METASTASIS, ROUS SARCOMA VIRUS, MARMOSSET (0200)
 METHYLCHOLANTHRENE, GUM ARABIC, BOVINE SERUM, GUINEA PIG (0946)
 3-METHYLCHOLANTHRENE, LYMPH NODE CELL, MOUSE (0471)

MONOACETYL, 4-HYDROXYAMINOQUINOLINE,
 MICE (1359)
 MURINE, ANTIGENICITIES, 3-METHYL-
 CHOLANTHRENE (0468)
 4-NITROQUINOLINE-1-OXIDE, MICE (1357)
 180, DNA, PROLIFERATION KINETICS
 (1677)
 ORNITHINE DECARBOXYLASE ACTIVITY
 (0315)
 OSTEOSARCOMA, FEMORAL METAPHYSIS, RAT,
 RADIATION (0543)
 PAROSTEAL, OSTEOGENIC SARCOMA OF THE
 JAW (0535)
 POLYMERIZED N-NITROSO-2,2,4-TRIMETHYL-
 1,2-DIHYDROQUINOLINE, SUBCUTANEOUS
 TISSUE, RAT (0488)
 RADIATION, SCAPULA, AXILLA, HUMAN
 (0133)
 RETICULAR CELL, EPIPHARYNGEAL CANCER,
 EPITHELIAL CARCINOMA (0013)
 RETICULUM CELL, VIRUS, MOUSE (1075)
 RHODAMINE, GLUCOSE-6-PHOSPHATE
 DEHYDROGENASE ISOZYMES, LIVER, RAT
 (0035)
 ROUS SARCOMA VIRUS, VOLE (0642)
 ROUS VIRUS, CARR-ZILBER STRAIN, MOUSE,
 CHICK EMBRYO (2367)
 ROUS VIRUS, DEFECTIVE STRAIN, HELPER,
 CHICKEN EMBRYO (1947)
 SCHMIDT-RUPPIN ROUS VIRUS, THYMUS,
 CHICKEN (0656)
 SKELETAL, ANTISARCOMA ANTIBODY,
 IMMUNITY (0710)
 SNYDER-THEILEN FELINE, PROPAGATION IN
 HUMAN CELL CULTURES (1073)
 SOFT TISSUE, NEGRO, FIBROUS TISSUE
 SARCOMA (0273)
 STICKER'S TUMOR, ULTRASTRUCTURE, DOG
 (2107)
 SUBCUTANEOUS, CADMIUM CHLORIDE, RAT
 (0898)
 TRANSPLANTATION, IMMUNITY, YEAST,
 MOUSE (0705)
 TUMOR GROWTH, PATHOGENESIS (1729)
 TUMOR RECURRENCE, ROUS SARCOMA VIRUS
 GROWTH (0650)
 TUMOR-SPECIFIC ANTIGEN, MURINE,
 3-METHYLCHOLANTHRENE (0072)
 WEIGHT, SEX, TEMPERATURE (0292)
 X-RAY THERAPY, BREAST CANCER (0132)
 YOSHIDA ASCITES, HORMONE, TUMOR
 GROWTH, OVARIECTOMIZED RATS (1214)
 YOSHIDA ASCITES, LUNG CARCINOMA,
 METASTASIS PATTERN (0322)
 YOSHIDA SARCOMA CELLS, PENETRATION OF
 ANTI-TUMOR ANTIBODIES, IMMUNO-
 HEMOLYTIC ANEMIA (0709)

RDINIA
 TUMOR MORBIDITY DATA, PULMONARY CANCER
 INCIDENCE (0766)*

ALP
 TONGUE, NEOPLASIA, MINERAL OIL, WALNUT
 SHELL DYE, MOROCCO (1633)*

APULA
 SARCOMA, AXILLA, RADIATION, HUMAN (0133)

AR TISSUE
 ESOPHAGEAL STENOSIS, CAUSTIC AGENTS,
 EPITHELIOMA, MAN (1154)

SCLEROTIC FOCI, NEOPLASTIC TRANSFORMA-
 TION, LUNG (1153)

SCHISTOSOMIASIS
 HEPATOSPLENIC, SPLENIC FOLLICULAR
 LYMPHOMA (2122)
 S. HEMATOBIUM, BLADDER, CARCINOMA
 (0771)

SCROTUM
 CARCINOMA, MINERAL OILS, OCCUPATIONAL
 EXPOSURE (0859)
 CARCINOMA, OCCUPATIONAL FACTORS,
 INDUSTRIAL HYGIENE (0116)

SERUM
 ANTIGENS, LYMPHOID TUMOR, CHICKEN
 (2439)
 ANTILYMPHOCYTE, CHEMICAL CARCINOGEN,
 DIMETHYLBENZ(A)ANTHRACENE, LYMPHATIC
 URIDINE UPTAKE (0456)
 ANTILYMPHOCYTE, 7,12-DIMETHYLBENZ(A)-
 ANTHRACENE, BUCCAL POUCH, EPIDERMOID
 CARCINOMA (1541)
 ANTILYMPHOCYTE, 3-METHYLCHOLANTHRENE,
 MICE, IMMUNOSUPPRESSION (1540)
 ANTITHYMOCYTE, BAYOL-F, PLASMACYTOMA
 INDUCTION (0691)
 CANCER PATIENTS, GROUP-SPECIFIC
 PROTEIN CONCENTRATIONS (1569)
 PROTEIN, CELL GROWTH REGULATION,
 PROTEIN CONFORMATION (1673)
 PROTEIN CONCENTRATIONS, ANTIGEN-
 SENSITIZED MICE, PRECANCEROUS
 CHANGES (1587)

SEX
 CHROMATIN, UTERINE TUMOR CELLS,
 CYTOLOGY, HUMANS (1596)
 FISH, XIPHOPHORUS, CROSS BREEDING,
 MELANOMA (2522)
 MORTALITY RATIO, LEUKEMIA, EPIDEMI-
 OLOGY (0275)
 SUSCEPTIBILITY, CIGARETTE SMOKING,
 URINARY BLADDER CANCER (0511)
 TUMOR WEIGHT OF SARCOMA, TEMPERATURE
 (0292)

SILICONE
 AUGMENTATION MAMMAPLASTY, BENIGN TUMOR
 INCIDENCE (0986)*

SIPPLE'S SYNDROME
 THYROID, BREAST, CARCINOMA (2581)*

SKIN
 BENZO(A)PYRENE HYDROXYLASE, 3-METHYL-
 CHOLANTHRENE, RAT (0939)
 BURN SCARS, RADIATION THERAPY, BASAL
 CELL CARCINOMAS (0531)
 CANCER, CHRONIC LYMPHOCYTIC LEUKEMIA,
 ETIOLOGY (0318)
 CANCER, RESPIRATORY CANCER, OCCUPA-
 TIONAL HAZARD (1277)
 CANCER, SOLAR KERATOSIS, EXPOSURE TO
 SUNBURN (0269)
 CARCINOMA, TANZANIA, SQUAMOUS CELL
 CARCINOMA OF THE CERVIX (1176)
 CERVIX, BREAST, IRAN, EPIDEMIOLOGY
 (0284)
 COLLAGENASE, CARCINOGENESIS, DIA,
 MICE (1343)
 DIMETHYLBENZANTHRACENE, MELANOMA,
 HAMSTER (0118)*
 9,10-DIMETHYLBENZANTHRACENE, ARYL

HYDROCARBON HYDROXYLASE, 7,8-BENZO-
FLAVONE, MOUSE (0445)
7,12-DIMETHYLBENZ(A)ANTHRACENE, HAIR
FOLLICLE CYCLE, MOUSE (0443)
DNA REPLICATION, 7,12-DIMETHYLBENZ-
(A)ANTHRACENE, MICE (0931)
ECCRINE POROMA, NOSE, RADIATION, THUMB
(0134)
EPIDERMAL CHANGES, 10B(N,ALPHA)7LI
REACTION RADIATION (1384)
EPIDERMAL PAPILLOMAS, SHOPE PAPILLOMA
VIRUS (1522)
EPIDERMIS, LARGE-CELL ACANTHOMAS
(1585)
EPITHELIOMA, BOWEN'S DISEASE, ARSENIC,
HUMANS (1368)
FIBROBLASTS, CARCINOMA, NASOPHARYNX,
CERVIX (1562)
HEMANGIOMA, RADIATION-INDUCED, CASE
REPORT (1401)*
HETEROGENIZATION, GRAFT,
7,12-DIMETHYLBENZ(A)ANTHRACENE
(0057)
HETEROGENIZING VIRUS, GENETIC TRAIT
(0145)
HODGKIN'S DISEASE, INVASION MECHANISM
(0821)
LIPID METABOLISM, LIGHT, IRRADIATION
(1856)
LIPIDS, LABELED ACETATE INCORPORATION,
AFLATOXIN B1, HUMAN (0918)
LUNG, BONES, VINYL CHLORIDE, RAT
(2200)
MELANOMA, GENETICS, MAN (0830)*
METHYLCHOLANTHRENE, GLUTAMATE, SUCCIN-
ATE, LACTATE, ISOCITRATE, GLUCOSE-6-
PHOSPHATE DEHYDROGENASES, MOUSE
(0469)
MORPHOLOGY, 7,12-DIMETHYLBENZ(A)-
ANTHRACENE, 3-METHYLCHOLANTHRENE,
MOUSE (2189)
MOUSE SQUAMOUS EPITHELIUM, TOBACCO
SMOKE CARCINOGENESIS, EXPERIMENTAL
BIOASSAY SYSTEM (0977)
NEOPLASIA, LEUKOCYTIC ZINC CONTENT
(0787)
NEUTRAL FRACTION, CIGARETTE SMOKE,
BENZO(A)PYRENE, MICE (1798)
RADIATION, NEUTRON BEAM, SWINE (1385)
SARCOMA, OXYGEN CONSUMPTION, METHYL-
CHOLANTHRENE (0465)
SOUTHERN IRAN, CANCER INCIDENCE (2041)
SQUAMOUS CARCINOMAS, ANTITHYMOCYTE
SERUM, DMBA (1325)
SQUAMOUS CELL CARCINOMA, HAND, ARM,
SUNLIGHT (0997)
SQUAMOUS CELL CARCINOMA, TERTIARY
BUTYL HYDROPEROXIDE, 4-QUINOLINE-1-
OXIDE, MICE (0026)
SQUAMOUS CELL EPITHELIOMA, DNA,
CYTOPHOTOMETRY (1722)*
SUNLIGHT, SQUAMOUS CELL CARCINOMA,
CAT (2288)
SURGICAL LESIONS, HISTAMINE, WHOLE
BODY IRRADIATION, RAT (0139)*
TRANSFORMATION, SWEAT GLAND, TUMOR
(2575)*
TUMOR, 7,12-DIMETHYLBENZ(A)ANTHRACENE,

POLYINOSINIC ACID/POLYCYTIDYLIC
ACID RNA, MOUSE (0447)
TUMOR, 7,12-DIMETHYLBENZ(A)ANTHRACENE
X-RAY IRRADIATION, MOUSE (2219)
TUMOR, ERYTHROPOIETIN, 3-METHYL-
CHOLANTHRENE (2233)
TUMOR, 3-METHYLCHOLANTHRENE,
4-DEIMTHYLAMINOSTILBENE, RAT (0470)
TUMOR, 3-METHYLCHOLANTHRENE, VITAMIN
B12, MOUSE (2234)
TUMOR, RIBOFLAVIN DEFICIENCY,
7,12-DIMETHYLBENZ(A)ANTHRACENE
(0935)
TUMOR SUSCEPTIBILITY, METHYLCHOL-
ANTHRENE, CIRCADIAN RHYTHM, MICE
(0074)
TUMOR, 3,3'-DIMETHYLBENZIDINE,
SEBACEOUS GLAND, RAT (0023)
TUMOR, UV IRRADIATION, CROTON OIL,
ACETIC ACID, XYLENE (0545)
TUMORIGENESIS, COAL-TAR PITCH,
PETROLEUM ASPHALTS (1330)
SMOKED FOOD
CARCINOGENESIS, REVIEW (0879)*
SODIUM
ONCONOGENESIS, DNA SYNTHESIS, MITOSIS
(1269)
SODIUM CYCLAMATE
CHOLESTEROL, CARCINOGENESIS EXPERIME
DESIGN (0512)*
SOLID FUEL CONSUMPTION
CANCER DEATH RATE, IMPORT RATES FOR
COFFEE, TEA (0280)
SPLEEN
ADOPTIVE TRANSFER, IMMUNITY, MICE
(2459)
CELLS, FRIEND VIRUS, PROTEIN SYNTHESIS
(1032)
DEFECTIVE IMMUNE RESPONSE, RIDGEWAY
SARCOMA IN MICE (1548)
EHRlich ASCITES TUMOR, IMMUNITY, MICE
(1999)
FOLLICULAR LYMPHOMA, HEPATOSPLENIC
SCHISTOSOMIASIS MANSONI (2122)
FRIEND LEUKEMIA VIRUS, GUAROA VIRUS,
ENHANCEMENT (0602)
FRIEND VIRUS, DEFECTIVE, HELPER (190)
FRIEND VIRUS, IMMUNITY (1902)
FRIEND VIRUS, LEUKEMIA (1022)
IMMUNE RESPONSE, BURSECTOMY, X-IRRA-
DIATION (1134)
IMMUNOSUPPRESSION, FRIEND LEUKEMIA
VIRUS, MOUSE (1529)
LACTIC DEHYDROGENASE PASSENGER VIRUS
RAUSCHER LEUKEMIA VIRUS, THYMIC
LYMPHOCYTE (0609)
LEUKEMIA, FRIEND VIRUS, PARABIOSIS
(1453)
LEUKEMIA, MOUSE (2552)
LEUKEMOGENIC VIRUS, MOUSE, WHOLE BODY
IRRADIATION (0592)
LYMPHOCYTES, IRRADIATED BONE MARROW
LYMPHOCYTES, CYTOMETRIC STUDY (053)
LYMPHOCYTES, TUMOR (2429)
LYMPHOID CELLS, INHIBITION OF TUMOR
GROWTH, ADENOVIRUS TYPE 12 (0617)
LYMPHOID TUMORS, ANTITHYMOCYTE SERUM
POLYOMA VIRUS (0682)

MURINE SARCOMA VIRUS, PLASMA VARIANT (0196)
 POLYRIBOSOME, RAUSCHER VIRUS, MOUSE (0607)
 REGRESSION OF SPLENOMEGALY, FRIEND LEUKEMIA VIRUS, DOUBLE-STRANDED PENICILLIUM RNA (1450)
 RETICULUM CELL SARCOMAS, ANTIGEN, AGE, MICE (2001)
 RNA, RAUSCHER VIRUS, MOUSE (1038)
 SHEEP ERYTHROCYTE IMMUNIZATION, VIRUS, RAUSCHER LEUKEMIA VIRUS (0174)
 SPLENECTOMY, BONE MARROW TRANSPLANTATION, RADIATION INJURY (0533)
 SPLENECTOMY, THYMECTOMY, MAMMARY TUMORIGENESIS (0628)
 SPLENOMEGALY, HARVEY MURINE SARCOMA VIRUSES, HELPER VIRUS FUNCTIONS (1935)
 THYMUS, LYMPH NODES, PHYTOHEMAGGLUTININ (1122)
 ULTRASTRUCTURE OF ANTIBODY-FORMING CELLS, FRIEND LEUKEMIA VIRUS, MOUSE (1535)

TERIGMATOCYSTIN
 HEPATOCELLULAR CARCINOMA, RATS (0402)

STEROID
 ADRENOCORTICAL VIRILIZING CARCINOMA (1642)
 CONTRACEPTIVE, VAGINAL CYTOLOGY, ESTRUS CYCLE (0120)*
 7,12-DIMETHYLBENZ(A)ANTHRACENE, CORTISONE ACETATE (0451)
 ESTRADIOL-17 BETA, LYMPHOID CELL PROLIFERATION, ACUTE LYMPHOBLASTIC LEUKEMIA, LYMPHOSARCOMA, MAN, IN VITRO (0342)
 SYNTHESIS, ADRENAL CARCINOMA, HUMAN (0782)

STILBESTROL
 MATERNAL THERAPY, VAGINAL ADENOCARCINOMA (1831)

STOMACH
 ADENOCARCINOMA, SURFACTANT, 4-NITROQUINOLINE-1-OXIDE, RAT (0095)
 ADENOMA, N-METHYL-N-NITROSO-N'-ACETYLUREA, PYLORUS, RAT (0483)
 ARGYROPHIL CELLS, NEOPLASIA, COLON (1590)
 CANCER, ANTIGENS, EMBRYONAL TISSUE, MAN (0707)
 CANCER, FIBROSIS, X-RAY THERAPY (0136)
 CANCER, INDUCTION IN DIFFERENT REGION, 20-METHYLCHOLANTHRENE (0947)
 CANCER, SOY BEAN PASTE CONSUMPTION, KOREA (1174)
 CARCINOMA, GASTRIC SURGERY, PEPTIC ULCER (1711)*
 CARCINOMA, GERMANY, MORTALITY, DETECTION (0765)*
 FORESTOMACH PAPILLOMA, URETHAN (0100)
 GASTRIC CANCER, NITROSAMIDES (1819)
 GASTRIC CARCINOMA, MUCOSA, HISTOCHEMICAL STAINING PROPERTIES, HUMAN (1217)
 GASTRIC CARCINOMA, NUCLEAR BOMB RADIATION (1172)
 GASTRIC CARCINOMA, STOMACH SURGERY (0528)

GASTRIC CARCINOMA, VITILIGO, ANEMIA (0777)
 GASTRIC MUCOSA, GENESIS OF POLYP, ADENOMATOUS POLYP (1155)
 GASTRIC SECRETION, MUCOSAL SEROTONIN LEVEL, NICOTINE, ATROPINE (0502)
 GASTRIC ULCER, MALIGNANT CHANGE (2031)*
 N-METHYL-N'-NITRO-N-NITROSOGUANIDINE, VAGOTOMY, SPLANCHNICOTOMY, TUMOR, RAT (2251)
 METHYL-NITROSOBIURET, CANCER, RAT (2252)
 N-METHYLUREA, N-METHYL-N-NITROSOUREA, RAT (1820)
 MOUSE GASTRIC CYSTS, LEIOMYOSARCOMA, N-METHYL-N'-NITRO-N-NITROSOGUANIDINE (1354)
 NEOPLASM, LEUKEMIA, N-(4-(5-NITRO-2-FURYL)-2-THIAZOLYL)ACETAMIDE (0417)
 NITROSOAZETIDINE, NITROSOHEPTAMETHYLENEIMINE, LUNG (0086)
 N-NITROSODIMETHYLAMINE, MASTOMYS (0958)
 N-(BETA-CHLOROETHYL)-N-NITROSOURETHAN, LUNG, TUMOR, RAT (2256)
 POLYPS, CARCINOMA (2569)
 TUMORS, METHYLNITROSOUREA, METHYL-NITROSOURETHAN (1823)
 ULCERS, CANCER, N-METHYL-N'-NITRO-N-NITROSOGUANIDINE (0093)

STREPTOZOTOCIN
 PANCREAS, TUMOR, RAT (2186)

STRESS
 ADRENAL LESIONS, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, RAT (2217)
 STOMACH ULCERS, CANCER, N-METHYL-N'-NITRO-N-NITROSOGUANIDINE (0093)

STRUCTURE
 ACTIVITY RELATIONSHIP, CARCINOGEN, 8,9-BENZO-GAMMA-CARBOLINE, 12H-PYRIDO(2,3-A)THIENO(2,3-I)CARBAZOLE, MOUSE (0411)
 ACTIVITY RELATIONSHIP, MONONITROQUINOLINES, HUCKEL (1826)
 ACTIVITY RELATIONSHIP, PHENOL COMPOUNDS, HAMMETT-TAFT EQUATION, REVIEW (0347)

SUBMAXILLARY GLAND
 POLYOMA, VIRUS, CHROMOSOME (1512)

SULFAMYLON
 ALPHA-AMINO-P-TOLUENESULFONAMIDE, LYMPHOCYTE TRANSFORMATION, DNA SYNTHESIS, HUMAN (0508)

SULTONES
 1,3-PROPANE SULTONE, 1,4-BUTANE SULTONE, NEUROGENIC TUMORS, RATS (0905)

SUNBURN
 SOLAR KERATOSIS, SKIN CANCER (0269)

SURFACTANT
 4-NITROQUINOLINE-1-OXIDE, STOMACH ADENOCARCINOMA, RAT (0095)
 NONIONIC, LYSOSOMAL CHANGES, TUMOR METASTASES (1680)

SURGERY
 GASTRIC, RECTAL CANCER, ESOPHAGEAL CANCER (1228)

SUPPRESSION OF IMMUNOCOMPETENCE,
CARCINOMA PATIENTS (1116)

SUSCEPTIBILITY
GENETIC, LIVER BILE DUCTS, SPONTANEOUS CHOLANGIOMA, MICE (1695)
INHERITED, FRIEND LEUKEMIA VIRUS, RESISTANT STRAIN (0169)
LONG-TERM CELL CULTURE, RAT, VIRUS (1412)
NEOPLASM, 7,12-DIMETHYLBENZ(A)ANTHRACENE (0063)
NITROSAMINE, GUINEA PIG (2152)
SPECIES-SPECIFIC VIRUS, INFECTION OF HUMAN-MOUSE HYBRID CELLS, VIRUS (1507)
VIRUS, PATHOLOGICAL RABBIT TISSUE (1963)

SYNDROME
CUSHING'S, HORMONAL TREATMENT, CARCINOMA, BILATERAL HYPERPLASIA, ADRENALECTOMY (0741)
GARDNER'S, TUMOR, MAXILLAR (1601)*
MEDICAL, MALIGNANCIES, SYMPTOM ASSOCIATION (0011)
REYE'S, TOXIC REACTION IN MONKEYS, AFLATOXIN B1 (1777)
SEZARY, ATYPICAL LYMPHOID CELLS, PRELYMPHOMATOUS CONDITION (1206)
TURNER'S, EXTRAGONADAL TUMOR, NEUROBLASTOMA, GANGLIONEUROMA (0012)

SYNERGISM
LEUKEMOGENESIS, GROSS LEUKEMIA VIRUS, X-IRRADIATION (0604)
LIVER, NITROSAMINES, RATS (0435)

TAR
CIGARETTE SMOKING, LUNG CANCER (0286)

TEMPERATURE
ASPERGILLUS FLAVUS, AFLATOXIN PRODUCTION (0519)*
EFFECT, DNA SYNTHESIS, THERMOSENSITIVE, SV40, VIRUS, MUTANT (1090)
EFFECT, POLYHEDRAL CYTOPLASMIC DEOXYRIBOVIRUS, VIRUS REPLICATION (0189)
FROG, VIRUS, HERPES, LUCKE ADENOCARCINOMA (2340)
LOW, LYMPHOCYTE, HUMAN, PHYTOHEMAGGLUTININ (0237)
VARIATION, EPIDEMIOLOGY, REGIONAL CANCER MORTALITY (1617)
VIRAL REPLICATION, SV40, MUTANT (0666)

TERATOCARCINOGENESIS
GENITAL SLICE GRAFT, TEMPERATURE, TESTES (0304)

TERATOGENESIS
DIMETHYLNITROSAMINE, TRANSPLACENTAL, RAT (1811)
SMOKING, KLINEFELTER'S SYNDROME (0376)
CHICK EMBRYOS, MYCOTOXINS (1779)

TRANSPLANTATION
CROWN GALL, GLUTAMINE (1694)
EMBRYO IMPLANTATION, ULTRASTRUCTURE, MURINE (1671)
MOUSE EGG CYLINDER, EXTRAUTERINE TRANSPLANTATION (0317)

TERPHENYL
NEOPLASM, REACTOR COOLANT (0111)

TESTES

DIMETHYLNITROSAMINE, RAT (2240)
EMBRYONAL ADENO CARCINOMA, CHILDREN, HISTOGENESIS (0746)
GERMINATIVE (2573)*
TERATOCARCINOGENESIS, GENITAL SLICE GRAFT, TEMPERATURE (0304)
TESTICULAR TUMOR, MORTALITY, TREATMENT, MAN (1186)
TUMORS, MALIGNANT TROPHOBLASTIC TERATOMA, TUMOR SPREAD (2116)

TESTICLE
PROSTATE, CARCINOMA, HUMAN (2572)

TESTOSTERONE
7,12-DIMETHYLBENZ(A)ANTHRACENE, CASTRATED AND INTACT HAMSTERS (0449)
MAMMARY ADENOCARCINOMA, ESTROGEN (0448)
RADIATION, HEMATOPOIETIC REGENERATION (1848)

THIAMINE
DIETARY BRACKEN FERN, DEVELOPMENT OF BLADDER TUMORS (0899)

THIOACETAMIDE
LIVER, CHROMOSOMES (1297)
LIVER TUMORS, METABOLIC CHANGES (0970)
LIVER TUMORS IN MICE (0969)
RIBOSOMAL FERRITIN, RAT LIVER (0475)
RNA METABOLISM, AMINE SYNTHESIS (0039)
RNA METABOLISM, LIVER (1775)

THOROTRAST
KIDNEY, HUMANS (1404)*
LYMPHOSARCOMA, CHROMOSOMAL ABERRATIONS, MAN (0137)
131I-LIPODOL, CARCINOGENIC EFFECTS, REVIEW (0845)
RADIATION, RETROMANDIBULAR DAMAGE, THOROTRASTOMA (1862)*
RADIUM KINETICS, BONE MARROW-FREE SKELETON, MODEL, RABBIT (1403)*

THYMUS
ALTERATIONS, CANCER AT VARIOUS SITES, REVIEW (1271)
CELL CULTURE, LEUKEMIA, MOUSE (0599)
CELL PROLIFERATION, FREUND'S ADJUVANT GUINEA PIG (1307)
CHICKEN, SARCOMA, SCHMIDT-RUPPIN ROUS VIRUS (0656)
CULTURE, RAT, MOLONEY LEUKEMIA VIRUS, C PARTICLES (1447)
EXTRACT, RESISTANCE TO TUMOR GROWTH, MURINE SARCOMA VIRUS (0197)
IMMUNE RESPONSE, CARCINOGENESIS, REVIEW (1272)
IMMUNOLOGY, LYMPHOCYTES, IRRADIATION (0842)
IRRADIATION, TUMORS, CHILDHOOD (1396)
LEUKEMIA, HAMSTER, PAPOVA VIRUS (0672)
LYMPHOID TISSUE ANTIGEN, LEUKEMIA, LYMPHOMA (1121)
LYMPHOMA, CELL-FREE SUPERNATANTS, GENETIC SUSCEPTIBILITY (0594)
LYMPHOMA, MURINE LEUKEMIA VIRUS, ALKALINE PHOSPHATASE, RAT (0590)
LYMPHOMA INDUCTION, DOSE RESPONSE, URETHAN (1829)

LYMPHOSARCOMA, IMMUNOLOGY, ORGAN TRANSPLANT, MAN (0360)
 LYMPHOSARCOMA, MAMMARY ADENOCARCINOMA, 4(5)-(3,3-DIMETHYL-1-TRIAZENO)-IMIDAZOLE-5(4)(CARBOXAMIDE (0423)
 MICE, PHYTOHEMAGGLUTININ (1573)
 NEONATAL, ANTILYMPHOCYTE SERUM THERAPY, IMMUNE DEFICIENCY, ONCOGENICITY, REVIEW (0357)
 PIKE, LYMPHOSARCOMA (2126)
 RADIOSTRONTIUM, HAEMATOPOIESIS, SPLEEN, BONE MARROW (1379)
 SPLEEN, MAMMARY TUMOR, MOUSE (2344)
 SPONTANEOUS LUNG TUMOR, IMMUNITY, MICE (2430)
 THYMECTOMY, ACUTE RADIATION, MICE (1001)
 THYMECTOMY, INFLUENCE OF MOUSE STRAIN, MAMMARY TUMORIGENESIS (0192)
 THYMECTOMY, MAMMARY TUMORIGENESIS, SPLENECTOMY (0628)
 THYMECTOMY, VIRAL TUMORIGENICITY, HAMSTER (1961)

THYROID
 ADENOCARCINOMA, METASTATIC PATTERN, HUMAN (0823)
 BREAST, CARCINOMA, SIPPLE'S SYNDROME (2581)*
 CARCINOMA, CHILDREN, EPIDEMIOLOGY AND CLINICAL COURSE (1173)
 CARCINOMA, JAPANESE, HAWAII, INCIDENCE (2486)
 CARCINOMA, ULTRASTRUCTURE (1714)*
 C-CELL ADENOMA, MEDULLARY CARCINOMA, FLUOROGENIC AMINES (1654)
 CHRONIC, TRYPAN BLUE, RAT, AGE, SEX (0034)
 EPIDERMAL CYST, ESTRADIOL, RAT, CASTRATION (0416)
 HYPERTHYROIDISM, HYPERPLASIA, SMALL INTESTINE, RAT (0740)
 IATROGENIC CANCER, RADIOACTIVE IODINE (0549)
 MALIGNANT ADENOMA, X-RAY (0135)
 MEDULLARY CARCINOMA, CALCITONIN ACTIVITY, FAMILIAL PHEOCHROMOCYTOMA (0803)
 MEDULLARY CARCINOMA, NORMAL CHROMOSOMES (1710)*
 MEDULLARY CARCINOMA, PRE-AMYLOID SUBSTANCE, AMYLOID STROMA (2111)
 NEOPLASIA, RADIOACTIVE IODINE EXPOSURE, BOMB FALLOUT (0529)
 NEOPLASTIC THYROID, IODINE, HUMAN (1635)
 PAPILLARY ADENOCARCINOMA, IODINE 131 (0126)
 PAPILLARY CARCINOMA (0789)
 PAPILLARY FOLLICULAR TUMOR, IMPLANTS, DIFFERENTIATION, RAT (2562)
 PRECANCEROUS ALTERATIONS, GOITER, ADENOMA, HUMANS (2030)
 RADIATION-INDUCED NEOPLASMS, NODULAR GOITERS, RADIATION THERAPY (0138)*
 RAT, RADIOIODINE 131, FOLLICULAR ATROPHY (0125)
 THYROIDITIS, 3-METHYLCHOLANTHRENE (0944)

TUMOR, CYTOGENETICS, ENZYME, RAT (2557)
 TUMOR, RADIOACTIVE LABELING, PARTICULATE THYROID PROTEINS (0255)
 URINE, THYROCALCITONIN, MEDULLARY CARCINOMA (1638)

L-THYROXINE
 METHYLTHIOURACIL, 7,12-DIMETHYLBENZ-(A)ANTHRACENE, RAT (1790)

TOBACCO
 BRONCHIAL CARCINOMA, LOCALIZATION (0750)
 CANCER, SPONTANEOUS PNEUMOTHORAX, EMPHYSEMA, HYPERSENSITIVITY (1834)
 CANCER DEATH RATE, SOLID FUEL CONSUMPTION, IMPORT RATES FOR COFFEE, TEA (0280)
 CHEWING, BUCCAL MUCOSA, BETEL-NUT (0978)
 CHEWING, HISTOLOGY OF BUCCAL MUCOSA, BETEL-NUT CHEWING (0979)
 CHEWING, ORAL AND OROPHARYNGEAL CANCER, INDIA (1177)
 CIGARETTE SMOKE, 3,4-BENZO(A)PYRENE, METABOLISM OF CARCINOGEN (1796)
 CIGARETTE SMOKE, PULMONARY CELLS, GUINEA PIG (2261)
 CIGARETTE SMOKERS, ACCUMULATION OF THORIUM IN LUNGS, THORIUM 232 (1400)
 CIGARETTE SMOKING, BLADDER CANCER, LOWER URINARY TRACT CANCER (0976)
 CIGARETTE SMOKING, BRONCHIAL CARCINOMA, BEAGLE (0108)
 CIGARETTE SMOKING, CANCER INCIDENCE, CONNECTICUT (1611)
 CIGARETTE SMOKING, CANCER OF THE PANCREAS, MORTALITY RATES (1178)
 CIGARETTE SMOKING, HIGH-RISK GROUP, LUNG CANCER (0751)
 CIGARETTE SMOKING, URINARY BLADDER CANCER, SEX DIFFERENCE (0511)
 CIGARETTE TAR, CARCINOMAS, LYMPHOMA, NEWBORN ICR MICE (0105)
 CIGARETTES, MICE, PULMONARY CARCINOMA, SEX (1367)
 CIGARETTES, TUMOR PROMOTION, INSECTICIDE (1793)
 CILIOSTASIS, TECHNIQUE (0107)
 COCARCINOGEN, BENZO(A)PYRENE, SKIN, MOUSE (2204)
 CONDENSATES, ESTERASE ACTIVITY AREA TEST, CARCINOGENICITY (0499)
 CURSCHMANN SPIRAL, LUNG (0104)
 FILTERED CIGARETTES, BRONCHIOL-ALVEOLAR TUMORS IN DOGS (0973), (0974)
 HUMAN PLACENTA, BENZO(A)PYRENE HYDROXYLATION (1799)
 HYPERPLASIA, FOCAL PROLIFERATION, LUNG, RABBIT (1833)
 INDIA, ORAL CAVITY CARCINOMA (1624)
 LUNG, KIDNEY, MOUSE (0501)
 LUNG CANCER, EPIDEMIOLOGY (0286), (1741)
 LUNG CANCER, MORTALITY RATES (0017)
 LUNG CANCER MORTALITY, TWIN PAIR (0109)

LUNG CANCER PATHOGENESIS, ETIOLOGY (1597)
 MOSAIC VIRUS, POLYPHENOLS, CARCINOGENICITY (1836)*
 MOSAIC VIRUS, POLYPHENOLS, SMOKING, CARCINOGENICITY (1837)*
 NEUTRAL FRACTION, BENZO(A)PYRENE, SKIN, MICE (1798)
 RADIOACTIVE POLONIUM POTASSIUM, RADON, REVIEW (0382)*
 SMOKE, DEPOSITION, HAMSTERS, LUNGS, RADIOACTIVITY (1366)
 SMOKE CARCINOGENESIS, EXPERIMENTAL BIOASSAY SYSTEM, MOUSE SQUAMOUS EPITHELIUM (0977)
 SMOKE CONDENSATE, TUMORIGENESIS, PROMOTION (2260)
 SMOKING, EPIDEMIOLOGY, CARCINOMA OF THE TONGUE (0847)
 SMOKING, 4-(4'-NITROBENZYL)PYRIDINE, THIN LAYER CHROMATOGRAPHY (0106)
 SOLID FUEL CONSUMPTION, CANCER DEATH RATES (0280)
 SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK, ETIOLOGICAL FACTORS (0850)
 TERATOGENESIS, KLINEFELTER'S SYNDROME (0376)
 TWIN METHOD, CANCER INCIDENCE (0500)
 WOMEN CIGARETTE SMOKERS, RESPIRATORY FUNCTION, SPUTUM CYTOLOGY (0975)
 TONGUE
 CARCINOMA, EPIDEMIOLOGY, SMOKING (0847)
 NEOPLASIA, MOROCCO, INCIDENCE, WALNUT SHELL DYE (1633)*
 TOXICITY
 OILSEED PROTEINS, ANIMAL FEED AFLATOXIN, REVIEW (0387)*
 TOYOCAMYCIN
 VIRUS-INFECTED CHICK EMBRYO CELLS, RNA SYNTHESIS (1105)
 TRACHEA
 CILIOSTASIS, EXPERIMENTAL TECHNIQUE, EPITHELIUM, VITAMIN A DEFICIENCY, METAPLASIA, RAT (1209)
 MUCOSA, PAPILLOMATA, DIETHYLNITROSO-AMINE, GOLDEN HAMSTER (0480)
 PAPILLOMA, NUCLEIC ACIDS, DIETHYLNITROSAMINE, HAMSTERS (1349)
 TOBACCO SMOKE EXPOSURE (0107)
 TRANS-4-DIMETHYLAMINOSTILBENE
 DISTRIBUTION, RAT (2271)*
 TRANSFORMATION
 ABORTIVE, POLYOMA VIRUS, BHK 21 (1959)
 ADENOVIRUS, HAMSTER CELL LINE (0184)
 ANO-RECTAL FISTULA, CARCINOMA, MAN (0341)*
 ARGINASE, ANAEROBIC GLYCOLYSIS, EMBRYO CELLS (1143)
 AVIAN ROUS SARCOMA VIRUS, FUJINAMI SARCOMA VIRUS, RAT EMBRYO, IN VITRO (2363)
 AVIAN SARCOMA VIRUS, UV-IRRADIATION (0640)
 CELL, FOCUS FORMATION, AVIAN MYELOBLASTOSIS VIRUS (1891)
 DIMETHYLNITROSAMINE, REVERTANT, LIMITED LIFE-SPAN, HAMSTER EMBRYO CELL (0951)
 EFFICIENCY, SV40, RAUSCHER, RAT (2376)
 EMBRYONIC TISSUE CULTURES, ROUS SARCOMA VIRUS, GRAFT (0654)
 FUSIFORM CELL, ROUS SARCOMA VIRUS MUTANT (0649)
 HEMATOPOIETIC CELLS, AVIAN MYELOBLASTOSIS VIRUS (0583)
 HUMAN CELL CULTURE, KIRSTEN MURINE SARCOMA VIRUS, RAUSCHER MURINE LEUKEMIA VIRUS, HOST RANGE ALTERATIONS (2352)
 IN VITRO, MALIGNANT, AFLATOXIN B1, RAT LIVER (1312)
 IN VITRO, NON-CNCOGENIC DEFECTIVE SV-40, HAMSTER (2372)
 IN VITRO NEOPLASTIC, TUMORIGENICITY OF MOUSE CELL LINES (1229)
 LEUKEMIA HELPER VIRUS, MURINE SARCOMA VIRUS, AGAR SUSPENSION CULTURE (0195)
 LEUKEMIC, NORMAL MARROW CELL GRAFT (1201)
 LYMPHOCYTE, CYCLIC AMP (0702)
 LYMPHOCYTE, PERIODITE (1377)*
 MACROPHAGE, SV40 (1096)
 MALIGNANT, IN VITRO CULTURE OF RETINOBLASTOMA, RETINOBLASTOMA (1234)
 MALIGNANT, LACRIMAL GLAND TUMOR (1149)
 MALIGNANT, METABOLIC CHANGES, PHASES OF CELL GROWTH (0854)
 MECHANISM, CROWN-GALL MODEL, DNA (0263)*
 MURINE LEUKEMIA VIRUS, MURINE SARCOMA VIRUS, VIRUS, NONPRODUCER VIRAL CLONES (0638)
 MURINE SARCOMA VIRUS, CELL MULTIPLICATION (0636)
 NEOPLASTIC, EMBRYONIC SYSTEMS, EPIGENETIC PROCESSES, REVIEW (0392)
 NEWBORN HAMSTER CELL, CELL PROPERTIES MORPHOLOGY, KARYOTYPE (1241)
 NON-TRANSFORMING MUTANT, POLYOMA VIRUS, CELL MEMBRANE AGGLUTINATION (0680)
 OSTEOGENIC, FIBROBLASTS, XENOGENIC BONE TRANSPLANT (0738)
 POLYCYCLIC HYDROCARBONS, HAMSTER CELLS (2197)
 POLYOMA VIRUS, FIBROBLAST SUSPENSIONS SURFACE INTERACTIONS (2387)
 POLYOMA VIRUS, VIRUS GENERATION, IN VITRO (0667)
 PREMALIGNANT CONDITION, BENIGN PROSTATIC ADENOMA (0745)
 RAT EMBRYO, 7,12-DIMETHYLBENZ(A)-ANTHRACENE, RAUSCHER LEUKEMIA VIRUS (1326)
 REVERSAL, TUMOR DNA (1210)
 REVERSION, VIRUS (2155)
 ROUS SARCOMA VIRUS, HAMSTERS, IN VIVO IN VITRO (1481)
 ROUS VIRUS REPLICATION, GENOME SUBUNITS, CHICK EMBRYO FIBROBLASTS (1078)
 SPONTANEOUS, TRANSFORMING AGENTS, ANIMAL CELL TRANSFORMATION IN VITRO REVIEW (0390)*

SPONTANEOUS MALIGNANT, MOUSE FIBRO-
 BLASTS, DIFFUSION CHAMBER (1584)
 SUSCEPTIBILITY, VIRAL DNA, SV40 (0659)
 SV40 - ADENOVIRUS HYBRID, ANTIGEN
 (0615)
 SV40, POLYOMA VIRUS, GANGLIOSIDE
 ALTERATION (1091)
 SV40, VARIANT, DNA, HUMAN FIBROBLAST
 (1095)
 TUMOR-ANTIGEN PRODUCTION, SV40 (0349)
 VACCINE VIRUS, MOUSE EMBRYO CELLS
 (1415)
 VIRAL GENOME, TEMPERATURE SENSITIVE
 MUTANT (0205)
 VIRUS, ROUS SARCOMA, GLYCOLIPID (2359)
 TRANSMISSION
 MILK, GENETIC SUSCEPTIBILITY, VIRUS,
 MAMMARY TUMOR VIRUS (0631)
 TRANSPLANTATION PASSAGE IN DOGS,
 GUINEA PIG, CANINE LYMPHOSARCOMA
 (2132)
 TRANSPLANTATION TUMOR, CANINE MAST
 CELL TUMOR (2131)
 TUMOR, NERVE SEVERANCE TUMORIGENESIS,
 COCKROACH (1701)
 VERTICAL, LEUKOSIS-FREE CHICKENS,
 AVIAN LEUKOSIS VIRUS (1888)
 TRANSPLANTATION
 ADENOVIRUS 12, SV40, TUMOR, HAMSTER
 (2331)
 FAT TISSUE, BREAST CANCER, HUMAN
 (1010)
 MOUSE EGG-CYLINDER, TERATOMA (0317)
 ORGAN, DEVELOPMENT OF MALIGNANCY,
 IMMUNOSUPPRESSIVE THERAPY (1118)
 ORGAN, INDUCED IMMUNOLOGIC INSUFFI-
 CIENCY, MALIGNANT (0839)
 TUMOR, ENHANCEMENT, LYMPHOCYTES,
 SPLEEN, RAT (2429)
 TUMOR, METASTASES, FREUND ADJUVANT,
 RAT (2022)*
 TRANSPORT
 ACTIVE, LIVER, PERFUSION, AMINO ACIDS
 (0537)
 SUGAR, ROUS SARCOMA VIRUS, CHICK
 EMBRYO CELLS (0204)
 TRAUMA
 BONE, WHOLE BODY IRRADIATION,
 OSTEOGENIC SARCOMA, MOUSE (1863)*
 LUNG, CARCINOMA, PATHOGENESIS
 (1406)*
 NEUROMA, ULTRASTRUCTURE (1402)*
 STOMACH SURGERY, GASTRIC CARCINOMA
 (0528)
 TRICHOMONAS
 UTERINE CERVIX, CANCER (1265)*
 TRITIUM
 DNA MOLECULAR WEIGHT, LYMPHOMA, MOUSE
 (2291)
 TROPHOBLASTIC TUMOR
 CHORIOEPITHELIOMA, IMMUNOLOGY,
 PLATELET ANTIBODIES, LEUCOCYTE
 ANTIBODIES (0227)
 TRYPAN BLUE
 CHRONIC THYROIDITIS, RAT, SEX, AGE
 (0034)
 DIMETHYLBENZANTHRACENE, HODGKIN'S
 DISEASE, PATHOGENESIS (0019)*

TRYPTOPHAN
 METABOLISM, 3-HYDROXYANTHRANILIC ACID,
 EARLY BENZIDINE CARCINOGENESIS, RAT
 (0911)
 TUBERCULOSIS
 LUNG CANCER, FINLAND (2117)
 TUMOR
 ANGIOGENESIS FACTOR, TUMOR VASCULAR-
 IZATION, ISOLATION (1647)
 HEPATOBILIARY TRACT, MORTALITY,
 SOUTHERN ITALY (1630)*
 SPONTANEOUS, MOUSE (2502)
 ULTRASTRUCTURE, MOUSE (2500)
 TUMORIGENESIS
 AFLATOXINS, MYCOTOXINS, REVIEW (0388)*
 AVIAN TUMOR VIRUS, STRAIN MC29, CHICKS
 (0580)
 SV40, INHIBITION, IMMUNIZATION (0671)
 TYLOSIS
 CARCINOMA OF THE ESOPHAGUS, GENETIC
 LINKAGE (0776)
 ULTRASOUND
 HUMAN BLOOD CELL CULTURES, CHROMOSOMAL
 ABERRATIONS (0527)
 ULTRASTRUCTURE
 ACID CARBOHYDRATES, BLOOD LYMPHOCYTE
 CELL MEMBRANE, HUMAN LYMPHOID
 LEUKEMIA (2142)*
 AMYLOID DEPOSITS, BRONCHIAL ADENOMA,
 OAT-CELL CARCINOMA, MORPHOLOGY
 (1664)
 ANNULATE LAMELLAE, HUMAN NEUROBLASTOMA
 CELLS (1684)
 ANTIBODY-FORMING CELLS, MOUSE SPLEEN,
 FRIEND LEUKEMIA VIRUS (1535)
 BASAL CELL CARCINOMA, MELANIN,
 KERATINOCYTES (2106)
 BRONCHOGENIC CARCINOMA, SQUAMOUS
 EPITHELIUM (1662)
 CANINE GLIOMA, ROUS SARCOMA VIRUS
 (1484)
 CARCINOMA, THYROID (1714)*
 CARDIAC MYXOMA (1253)
 CAT CELL CARCINOMA, ACTH SYNDROME
 (2103)
 CILIA, PARATHYROID ADENOMA (1669)
 CLASSIFICATION, HERPES SIMPLEX VIRUS
 (0002)
 CLEAR CELL TUMORS, RENAL TUBULES,
 GLYCOGEN METABOLISM, RATS (1352)
 CONNECTIVE TISSUE, LYMPHOMA, THYMOMA
 (2113)
 CYTOLOGIC DIAGNOSIS, MAMMARY TUMOR,
 ATYPIA, ASPIRATION BIOPSY (0262)*
 DIMETHYLNITROSAMINE, ADENOCARCINOMAS
 (1809)
 DIMETHYLNITROSAMINE, RENAL MESENCHYMAL
 TUMOR, RAT (1807)
 EHRLICH ASCITES, MOUSE CEREBRUM, ACID
 PHOSPHATASE (1684)
 EPIDIDYMUS, MESOTHELIAL ORIGIN OF
 TUMOR, ADENOMATOID TUMOR (1161)
 GLOBULASTOMA HISTOCHEMISTRY, LACTATE
 PRODUCTION (1698)
 GLOMUS TUMOR, EPITHELIOID CELLS,
 HISTOGENESIS (1227)
 GOLGI APPARATUS, HUMAN MELANOMA,
 MITOSIS (0786)

- HEPATOCARCINOMA, MONKEY, N-NITROSO-DIETHYLAMINE (0955)
 HEPATOCYTE, RADIATION, PROTEIN-BOUND NEUTRAL HEXOSES (0546)
 HEPATOMA, AZO DYE, RAT (1785)
 HERPESVIRUS, INFECTIVITY, REVIEW (1759)
 HEXON, CRYSTALS, ADENOVIRUS (1913)
 HISTOPATHOLOGY, DEEP BRAIN LESIONS, PROTON-IRRADIATION (1007)
 HUMAN EPIDERMIS, SUNLIGHT EXPOSURE (1855)
 HUMAN GASTRIC MUCOSA, CARCINOMA, HISTOCHEMICAL STAINING PROPERTIES (1217)
 KERATINOCYTE, SQUAMOUS CELL CARCINOMA, DESMOSOMES, HUMANS (1231)
 LARYNX, PRECANCEROUS CHANGES, CHRONIC LARYNGITIS (1152)
 LEUKEMIA, GRAFFI VIRUS, MICE (1040)
 LEUKEMIA, MYELO-MONOCYTIC, MONOCYTIC, HUMAN (2115)
 LEUKEMOGENIC AND SARCOMAGENIC VIRUSES, VIRUS, PARTICLES (1866)
 LIVER, ETHIONINE NODULES, RAT (1296)
 LUNG, WHOLE BODY IRRADIATION, RAT (0128)
 LUNG CANCER, CLASSIFICATION, ELECTRON MICROSCOPE (0829)*
 LYMPHOBLAST, PHYTOHEMAGGLUTININ INDUCED TRANSFORMATION, IN VITRO, MAN (0242)*
 MALIGNANT CELLS, NUCLEAR POCKETS, NUCLEOLUS (1663)
 MEDIASTINAL LYMPHOMA, LUNG EPITHELIOMA URETHAN, GERM-FREE MOUSE (0494)
 MEDULLARY CARCINOMA, FLUOROGENIC AMINES, THYROID ADENOMA (1654)
 METASTASIS SEQUENCE, WALKER 256 TUMOR (1683)
 MORPHOLOGY OF TRANSFORMED CELLS, MAREK'S DISEASE VIRUS, HERPESVIRUS OF TURKEY (1465)
 MURINE TERATOMAS, EMBRYO IMPLANTATION (1671)
 MYOEPIHELIAL CELLS, ROLE IN NEOPLASIA (2035)*
 NEOPLASM, INTRACISTERNAL A-PARTICLES, VIRUS, MOUSE (1422)
 NEUROMA, TRAUMA (1402)*
 NUCLEAR BODIES, HUMAN TUMORS, DIFFERENTIATION CAPACITY (1672)
 NUCLEOCAPSID, AVIAN MYELOBLASTOSIS VIRUS (0587)
 OSTEOSARCOMA, 32 PHOSPHORUS (0548)
 PANCREATIC ISLET CELL ADENOMA (2105)
 RAT TUMOR CELLS, LOW MALIGNANCY, HIGH MALIGNANCY (1668)
 RNA VIRUS, NUCLEOCAPSID (0176)
 RODENT SARCOMAS, MOLONEY MURINE SARCOMA VIRUS (1930)
 ROUS SARCOMA VIRUS, ROUS ASSOCIATED VIRUS, VIRION CORE ANALYSIS (0206)
 RUSSELL'S VIPER, EDEMATOUS MYXOFIBROMA C-TYPE PARTICLE, VIRUS (1425)
 SALIVARY GLAND TUMOR, MYOEPIHELIAL CELLS (2163)
 STICKER'S TUMOR, DOG (2107)
 STORAGE CELL, GAUCHER'S DISEASE, CHRONIC MYELOGENOUS LEUKEMIA (2110)
 SV40, 6 TYPE POLYPEPTIDE (1497)
 SV40, STRUCTURAL PROTEINS (1953)
 TUMOR, PAROTID, PATHOGENESIS, HUMANS (2033)*
 TUMOR BUD CELL, SUPERFICIAL BASAL CELL CARCINOMA (0735)
 TUMOR CELL, MOUSE (2500)
 VIRAL PARTICLES, OVINE PULMONARY ADENOMAS (1411)
 YABA TUMOR POX VIRUS (1430)
 URETER
 LEUKOPLAKIA, CALCULUS (2141)*
 URETHAN
 ADRENAL TUMOR, ENDOCRINE LESION (0498)
 AGE, TUMOR SPECTRUM (0492)
 CARCINOGENESIS, PHENOBARBITAL, LUNG, MOUSE (0493)
 CARCINOGENICITY, ENHANCED DETECTION, TRANSPLACENTAL EFFECTS, MOUSE (0972)
 CARCINOGENICITY, GUINEA PIGS (0437)
 7,12-DIMETHYLBENZ(A)ANTHRACENE, GAMMA-IRRADIATION, HORMONE (1789)
 7,12-DIMETHYLBENZ(A)ANTHRACENE, IMMUNE RESPONSE IN RATS (1989)
 ENZYME INDUCER, LUNG, MOUSE (2255)
 HAMSTER, FORESTOMACH PAPILLOMA (0100)
 LUNG ADENOMA, RADIATION (0101)
 MALIGNANT MELANOMA INDUCTION (0497)
 MAMMARY GLAND TUMOR, SPLENECTOMY, THYMECTOMY (0099)
 MEDIASTINAL LYMPHOMA, LUNG EPITHELIOMA VIRUS PARTICLES, GERM-FREE MOUSE (0494)
 MEDIASTINAL LYMPHOMA, VIRUS-LIKE PARTICLES (0495)
 MOUSE HEPATOMAS, REGENERATION, MOUSE (0971)
 NUCLEIC ACIDS, PROTEIN, INTERACTION (1362)
 THYMIC LYMPHOMA INDUCTION, DOSE RESPONSE (1829)
 TUMOR INDUCTION, AGE, HAMSTERS (1361)
 TUMOR PROFILE, PERINATAL AGE PERIOD (0496)
 UROGENITAL TUMOR
 DNA POLYMERASE (0331)
 LOWER, BLADDER CANCER, CIGARETTE SMOKING (0976)
 UROPORPHYRIN
 EHRLICH ASCITES TUMOR CELLS (1702)
 UTERINE CANCER
 OVARIAN CANCER, UNITED STATES INCIDENCE (1619)
 UTERUS
 BREAST, DOUBLE MALIGNANCY (0299)*
 CANCER, CYTOLOGY, SEX CHROMATIN, HUMANS (1596)
 CARCINOMA, OBESITY, HYPERTENSION, DIABETES MELLITUS (1716)*
 CARCINOMA, PATHOGENESIS, REVIEW (0852)
 CERVIX, EPITHELIAL ATYPIA, COMBINED CONTRACEPTIVES, HUMAN (0514)*
 CHANGES, ESTROGEN TREATMENT, INTRA-UTERINE CONTRACEPTIVE DEVICE, RAT (0985)

ESTROGENS, POLYETHYLENE STRIPS, GUINEA PIG (0815)
 GONADAL DYSGENESIS, XY SEX CHROMOSOME, AMENORRHEA, MALIGNANCY (1261)
 MAMMARY GLAND CANCER, SOMATOTROPIN, GLUCOSE EFFECT, HUMANS (2469)
 3-METHYLCHOLANTHRENE, EPIDERMIZATION, MICE (1804)
 RADIATION, CARCINOGENICITY, RAT (1846)
 CCINE
 TUMOR, ANTIGENIC "OTHERNESS", CARRIER AGENTS (0356)
 GINA
 ADENOCARCINOMA, MATERNAL STILBESTROL THERAPY (1831)
 CARCINOMA, INCIDENCE, CONSTITUTION (2034)*
 CYTOLOGY, ESTRUS CYCLE, STEROID CONTRACEPTIVE (0120)*
 9,10-DIMETHYL-1,2-BENZANTHRACENE, SARCOMA, CARCINOMA (0441)
 EPITHELIUM, DIETHYL STILBESTROL, CERVIX (1294)
 GENITAL INFECTION IN CEBUS MONKEY, HERPESVIRUS HOMINIS (1061)
 CTOR
 COCKROACH, LYMPHOSARCOMA, TOAD (0565)
 NYL CHLORIDE
 SKIN, LUNG, TUMOR, RAT (2200)
 RUS
 ADENOVIRUS, CANAVANINE, INHIBITION OF REPLICATION (1046)
 ADENOVIRUS, CAPSID PROTEINS (1043)
 ADENOVIRUS, CHICK EMBRYO CELLS, INTERFERON INDUCTION (0178)
 ADENOVIRUS, CHROMOSOME ABERRATIONS (0686)*
 ADENOVIRUS, CRYSTALS, HEXON (1913)
 ADENOVIRUS, DNA SYNTHESIS, HAMSTER KIDNEY CELL, HUMAN EMBRYO LUNG CELL (1044)
 ADENOVIRUS, MAGNESIUM CHLORIDE, ENHANCED PLAQUE FORMATION (1053)
 ADENOVIRUS, PORCINE LEUKEMIA, STRONTIUM 90 (1838)
 ADENOVIRUS, RABBIT HEART FIBROBLAST CELL CULTURE, INFECTIOUS VIRUS FORMATION (0181)
 ADENOVIRUS, TRANSFORMATION OF HAMSTER CELL LINE (0184)
 ADENOVIRUS, TUMOR SPECIFIC TRANSPLANTATION ANTIGEN, ADENOVIRUS (0180)
 ADENOVIRUS 2, PROTEIN SYNTHESIS, METHIONINE INITIATION (1911)
 ADENOVIRUS 2, STRUCTURAL PROTEINS (1912)
 ADENOVIRUS 2, STRUCTURAL PROTEINS, DEGRADATION PRODUCTS (0613)
 ADENOVIRUS 2, SV40, HYBRID, DNA (1052)
 ADENOVIRUS 2, SV40, HYBRIDIZATION, DNA (2371)
 ADENOVIRUS 2, ULTRASTRUCTURE, INFECTED CELL (2330)
 ADENOVIRUS 5, ARGININE, PROTEIN, HUMAN CELLS (2328)
 ADENOVIRUS 5, TEMPERATURE-SENSITIVITY, MUTATION, 5-BROMODEOXYURIDINE (2327)
 ADENOVIRUS 7, ERYTHROCYTES, VIRAL ADSORPTION (0614)
 ADENOVIRUS SA7, TRANSFORMED CELLS, TRANSPLANTATION ANTIGEN, HAMSTER (0616)
 ADENOVIRUS 8, 9, IMMUNOLOGY (1054)
 ADENOVIRUS 12, ACTIVATION OF DNA SYNTHESIS IN HAMSTER CELLS (1047)
 ADENOVIRUS 12, ANTIGEN, HELA CELL (1981)
 ADENOVIRUS 12, CARBOHYDRATE METABOLISM RAT (2333)
 ADENOVIRUS 12, DEFECTIVE (1914)
 ADENOVIRUS 12, DEFECTIVE SIMIAN VIRUS 40, TUMORIGENICITY (1455)
 ADENOVIRUS 12, DNA SIZES (2325)
 ADENOVIRUS 12, DNA, KIDNEY CELLS (1051)
 ADENOVIRUS 12, RNA SYNTHESIS, INFECTION, HAMSTER (2329)
 ADENOVIRUS 12, HETEROKARYOCYTES, PERMISSIVE AND NONPERMISSIVE CELL FUSION (0611)
 ADENOVIRUS 12, SARCOMA, IMMUNOLOGY, HAMSTER (0618)
 ADENOVIRUS 12, SPLEEN LYMPHOID CELLS, INHIBITION OF TUMOR GROWTH (0617)
 ADENOVIRUS 12, SV40, TRANSPLANTATION, TUMOR ANTIGEN, HAMSTER (2331)
 ADENOVIRUS 12, T-ANTIGEN, AMINO ACID COMPOSITION, HAMSTER (1526)
 ADENOVIRUS 12, T-ANTIGEN, TUMOR, FREEZING (0177)
 ADENOVIRUS 12, T ANTIGEN, ULTRAVIOLET IRRADIATION (1978)
 ADENOVIRUS 12, TRNA METHYLASE, HAMSTER (1049)
 ADENOVIRUS 12, TUMOR CELL EXTRACTS, TRANSPLANTATION IMMUNITY (1055)
 ADENOVIRUS 12, TUMOR MORPHOLOGY, MOUSE (1456)
 ADENOVIRUS 12, 6, 3, RAT EMBRYO FIBROBLASTS, GLYCOLYSIS (1048)
 ADENOVIRUS 31, DNA, TEMPERATURE MUTANT (1458)
 ADENOVIRUS-SV40 HYBRIDS, SV40 ANTIGEN (1980)
 ADENOVIRUS, SV40, INHIBITION OF SUPERINFECTION (0612)
 ADENOVIRUS-ASSOCIATED VIRUS, ENHANCEMENT, HERPES SIMPLEX VIRUS (1056)
 ADENOVIRUS-ASSOCIATED VIRUSES, HUMAN HERPES VIRUS (0179)
 ADENOVIRUS TYPE, COCULTIVATION (2397)*
 ANAL WART, CARCINOMA IN SITU (2396)*
 A-TYPE VIRUS-LIKE PARTICLES, MURINE PLASMA CELL NEOPLASIA, PARAPROTEIN (0593)
 AVIAN ADENOVIRUS, CHICKEN-EMBRYO-LETHAL-ORPHAN, EPENDYMOMAS (0182)
 AVIAN ERYTHROBLASTOSIS, HETEROGENEITY, INFECTIVITY (1437)
 AVIAN LEUKEMIA, SPREAD, BIRD (2166)*
 AVIAN LEUKOSIS, ANTIGENS, IMMUNE RESPONSE, CHICKEN (1964)

- AVIAN LEUKOSIS, EPIZOOTIC, CELL PARTICLES (0324)
 AVIAN LEUKOSIS, RNA (1887)
 AVIAN LEUKOSIS, ROUS SARCOMA, HELPER (1439)
 AVIAN LEUKOSIS, ROUS SARCOMA, IMMUNOLOGIC CROSS-REACTION, GROUP SPECIFIC ANTIGEN, HUMAN LEUKEMIC PLASMA (1126)
 AVIAN LEUKOSIS, VERTICAL TRANSMISSION, LEUKOSIS-FREE CHICKENS (1888)
 AVIAN LEUKOSIS-SARCOMA, VIRUS SUSCEPTIBILITY, ERYTHROCYTE ISOANTIGEN (0160)
 AVIAN LEUKOSIS VIRUS MC29, PROPERTIES (1735)
 AVIAN MYELOBLASTOSIS, AMINO ACID ACCEPTOR RNA, AMINOACYLATION CAPACITY (0585)
 AVIAN MYELOBLASTOSIS, ANTIGEN, AMINO ACID (1027)
 AVIAN MYELOBLASTOSIS, ANTIGENICITY (1065)
 AVIAN MYELOBLASTOSIS, DNA POLYMERASE ACTIVITY, RNA (0584)
 AVIAN MYELOBLASTOSIS, FOCUS FORMATION, CELL TRANSFORMATION (1891)
 AVIAN MYELOBLASTOSIS, GROUP-SPECIFIC ANTIGEN (0582)
 AVIAN MYELOBLASTOSIS, NUCLEOCAPSID STRUCTURE (0587)
 AVIAN MYELOBLASTOSIS, OLIGOMER, MITOCHONDRIA, DNA (2308)
 AVIAN MYELOBLASTOSIS, POLYMERASE, RNA, DNA (0586)
 AVIAN MYELOBLASTOSIS, POLYRIBOSOMES, RNA, CHICKEN (1026)
 AVIAN MYELOBLASTOSIS, PROTEIN COMPONENTS (1064)
 AVIAN MYELOBLASTOSIS, TRANSFORMATION, HEMATOPOIETIC CELLS (0583)
 AVIAN SARCOMA, LETHAL MUTANTS TS 75 AND 149 (1478)
 AVIAN SARCOMA, NONTRANSFORMANTS, RNA DIFFERENCES (1066)
 AVIAN SARCOMA, ROUS, FUJINAMI, RAT EMBRYO CELLS, IN VITRO (2363)
 AVIAN SARCOMA, TRANSFORMED RAT CELLS, GENOME (1488)
 AVIAN SARCOMA, UV IRRADIATION, TRANSFORMING CAPACITY (0640)
 AVIAN SARCOMA, VISIBLE LIGHT, 5-BROMODEOXYURIDINE, CHICK EMBRYO FIBROBLAST (0641)
 AVIAN TUMOR, PROTEIN COMPONENTS, SURFACE ANTIGENS (1085)
 AVIAN TUMOR, RNA, NUCLEOTIDE COMPOSITION, HYBRIDIZATION (1942)
 AVIAN TUMOR, ROUS SARCOMA VIRUS, GLYCOPROTEIN COMPONENT (0202)
 AVIAN TUMOR, STRAIN MC29, TUMORIGENESIS, CHICKS (0580)
 AVIAN TUMOR, TOYOCAMYCIN, CHICK EMBRYO CELLS, RNA SYNTHESIS (1105)
 B AND C PARTICLES, MAMMARY GLAND CANCER, LEUKEMIA, IMMUNOLOGY, MOUSE (2410)
- BAI AVIAN LEUKOSIS, RNA, TRANSMISSION OF MYELOBLASTOSIS (1890)
 BERGOLZ, RETICULOSARCOMATOSIS, FREUND'S ADJUVANT, MOUSE (1477)
 BOVINE LYMPHOSARCOMA (1873)
 BOVINE LYMPHOSARCOMA, CYTOPATHIC EFFECT IN MIXED CELL CULTURE (1876)
 BOVINE LYMPHOSARCOMA, TRANSMISSION OF DISEASE (2129)
 BOVINE SYNCYTIAL, LYMPHOSARCOMATOUS CATTLE, MORPHOLOGICAL VIRAL VARIANT (0563)
 BOVINE SYNCYTIAL, VIRUS INFECTION IN SEVERAL SPECIES (1875)
 BURKITT'S LYMPHOMA, IMMUNOSUPPRESSION (0687)*
 BURKITT'S LYMPHOMA, INCIDENCE, REVIEW (0870)*
 BURKITT'S LYMPHOMA, MALARIA (0006)
 C-TYPE, GS ANTIGEN, LEUKEMIA, RODENT (2457)
 C-TYPE, MAMMALIAN, ANTIGENIC SPECIFICITY (2407)
 C-TYPE PARTICLE, LEUKEMIC COW LYMPHOCYTES, BOVINE LYMPHOCYTOSIS (1877)
 C-TYPE PARTICLE, LIVER, FIBROBLASTS (1413)
 C-TYPE PARTICLE, MAMMARY TUMORS, LEUKEMIA, RAT (1870)
 C-TYPE PARTICLE, PIG KIDNEY CELLS (1428)
 C-TYPE PARTICLE, RUSSELL'S VIPER, EDEMATOUS MYXOFIBROMA (1425)
 C-TYPE RNA, DNA POLYMERASE ACTIVITY (0555)
 C-TYPE SARCOMA, B-TYPE MOUSE MAMMARY TUMOR, LEUKEMIA, POLYMERASE (0589)
 C-TYPE VIRUS PARTICLES, ENVELOPE SPIKES, FELINE LYMPHOMA (0588)
 CANCER, IMMUNITY, REVIEW, RATS, MICE, BIRDS (1734)
 CANCER VIRUS, NUCLEIC ACIDS-HYBRIDIZATION (0554)
 CANCER VIRUS, SV40, NEW CELL LINES, KIDNEY (1501)
 CELL-FREE FILTRATE, ANTIGEN, FOCUS FORMATION, HUMAN SARCOMAS IN VITRO (1427)
 CELL-FREE ORGAN EXTRACTS, MURINE MYELOID LEUKEMIA, LEUKEMIA INDUCTION (0605)
 CELL-FREE THYMIC SUPERNATANTS, GENETIC SUSCEPTIBILITY, THYMIC LYMPHOMA (0594)
 CELL SENSITIVITY, PATHOLOGICAL RABBIT TISSUE (1963)
 CHICK-EMBRYO-LETHAL-ORPHAN, ANTIGENICITY (2303)
 CHICK-EMBRYO-LETHAL-ORPHAN, ANTIGENS, CHICK KIDNEY CELLS (1417)
 CHICK-EMBRYO-LETHAL-ORPHAN, ONCOGENICITY, HAMSTER (0208)
 CHICK-EMBRYO-LETHAL-ORPHAN ADENOVIRUS, TUMORS, HISTOPATHOLOGY (1459)
 CHIKUNGUNYA, FIBROBLASTS, LEUKEMIA INTERFERON (1628)

CHROMOSOME ABERRATIONS, VIRAL INDUC-
TION (0866)*
CIRCUMCISION, VENEREAL DISEASE,
PROSTATE (2394)*
COMMON ANTIGEN, MAREK'S DISEASE
HERPES, EPSTEIN-BARR (1028)
COMPARISON, BOVINE LEUKOTIC VIRUS-LIKE
PARTICLES, FELINE LEUKOSIS VIRUS
(1874)
CYTOMEGALO, PARANGLIOMA, HUMAN
(2302)
CYTOMEGALOVIRUS, JUVENILE XANTHO-
GRANULOMA (1518)*
DEFECTIVE, MOLONEY SARCOMA, MAZURENKO
LEUKEMIA, MOUSE (1475)
DENSONUCLEOSIS, ONCOGENICITY, DNA
SYNTHESIS (0221)*
DIGITAL FIBROUS TUMOR, CYTOPLASMIC
INCLUSIONS (0795)
DNA, POLYMERASE, BIRD (1943)
DNA, POLYMERASE, MC29 TUMOR (1892)
DNA, POLYMERASE, RNA, MILK, HUMAN
(1878)
DNA VIRUS-INDUCED ANIMAL TUMORS, HUMAN
MAMMARY CARCINOMA, TUMOR-SPECIFIC
NEOANTIGEN (1131)
DNA VIRUS-TRANSFORMED CELL LINES,
ENZYMATIC BLOCK, GANGLIOSIDE SYNTHESIS
(0568)
EFFECT ON IMMUNE SYSTEM, RETICULOENDO-
THELIAL SYSTEM (0882)*
ENVIRONMENTAL CARCINOGENS, BOTTOM-
FEEDING FISH, OYSTERS, COMPARATIVE
ONCOLOGY (1273)
EPSTEIN-BARR, ANTIBODIES, BURKITT'S
LYMPHOMA (1973)
EPSTEIN-BARR, ANTIBODY, CARCINOMA,
NASOPHARYNX (2463)*
EPSTEIN-BARR, ANTIBODY TITERS,
HODGKIN'S DISEASE (1025)
EPSTEIN-BARR, ANTIBODY TITERS, MACAQUE
MONKEYS (1974)
EPSTEIN-BARR, ANTIGEN, CLONED HUMAN
LEUCOCYTES (1021)
EPSTEIN-BARR, ANTIGENS, LYMPHOID CELLS
(0156)
EPSTEIN-BARR, BURKITT'S LYMPHOMA
(1432)
EPSTEIN-BARR, BURKITT'S LYMPHOMA,
AUTOIMMUNE SYSTEM, MALARIA (0005)
EPSTEIN-BARR, BURKITT'S LYMPHOMA,
MORPHOLOGY (0575)
EPSTEIN-BARR, BURKITT'S LYMPHOMA,
NASOPHARYNGEAL CARCINOMA (1024)
EPSTEIN-BARR, BURKITT'S LYMPHOMA,
NASOPHARYNGEAL CARCINOMA, DNA (0574)
EPSTEIN-BARR, BURKITT'S LYMPHOMA,
VIRUS ANTIBODY IN TAIWAN MONKEY
(1972)
EPSTEIN-BARR, BURKITT'S LYMPHOMA CELLS
(1886)
EPSTEIN-BARR, BURKITT'S LYMPHOMA CELLS
NEOCARZINOSTATIN (1020)
EPSTEIN-BARR, BURKITT'S LYMPHOMA SERUM
ANTIBODY, NASOPHARYNGEAL CARCINOMA
SERUM ANTIBODY (0153)
EPSTEIN-BARR, C MARKER CHROMOSOME
(0576)

EPSTEIN-BARR, CHROMOSOME, ABERRATION
(2307)
EPSTEIN-BARR, DNA, METAPHASE CHROMO-
SOMES (1881)
EPSTEIN-BARR, DNA STIMULATION,
LEUKOCYTE (1884)
EPSTEIN-BARR, GROWTH OF TRANSFORMED
LEUKOCYTES IN VITRO (1883)
EPSTEIN-BARR, HERPES SIMPLEX, CYTO-
MEGALOVIRUS, ANTIBODY, HODGKIN'S
DISEASE (0155)
EPSTEIN-BARR, HODGKIN'S DISEASE,
ANTIBODY TITERS (1434)
EPSTEIN-BARR, HUMAN EMBRYONIC CELL
LINE, LEUKEMIA (0570)
EPSTEIN-BARR, HUMAN LEUKEMIC CELLS
(1882)
EPSTEIN-BARR, HUMAN LYMPHOBLASTOID
CELL (1435)
EPSTEIN-BARR, INFECTIOUS MONONUCLEOSIS
(0353), (0577)
EPSTEIN-BARR, INFECTIOUS MONONUCLEOSIS
ACUTE LYMPHOCYTIC LEUKEMIA (1578)
EPSTEIN-BARR, INFECTIOUS MONONUCLEO-
SIS, BURKITT LYMPHOMA, LEUKEMIA (0004)
EPSTEIN-BARR, INFECTIOUS MONONUCLEO-
SIS, BURKITT TUMOR (0154)
EPSTEIN-BARR, JUVENILE BURKITT
LYMPHOMA, NECK, GERMANY (0152)
EPSTEIN-BARR, LYMPHOBLASTOID CELLS,
COMPLEMENT-FIXING ANTIGENS,
BURKITT'S LYMPHOMA (1532)
EPSTEIN-BARR, LYMPHOBLASTOID CELL
LINES, CYTOGENETICS (1885)
EPSTEIN-BARR, LYMPHOCYTE INDUCTION,
MAN (2421)
EPSTEIN-BARR, LYMPHOMA, INFECTIOUS
MONONUCLEOSIS (0875)*
EPSTEIN-BARR, MAREK'S DISEASE, HERPES,
ANTIGENIC CROSS-REACTIVITY (1466)
EPSTEIN-BARR, MEMBRANE ANTIGEN,
BURKITT'S LYMPHOMA, NASOPHARYNGEAL
CARCINOMA (0578)
EPSTEIN-BARR, MYELOGENOUS LEUKEMIA,
MULTIPLE NYELOMA, ALL SURFACE (1433)
EPSTEIN-BARR, NASOPHARYNGEAL CARCINOMA
SURFACE ANTIGEN (0579)
EPSTEIN-BARR, SERUM ANTIBODY TITRATION
(0757)
EPSTEIN-BARR, SERUM ANTIBODY TITRATION
CHILDREN (0758)
EPSTEIN-BARR, TUMOR MEMBRANE ANTIGENS,
BURKITT'S LYMPHOMA (1739)
EPSTEIN-BARR, VIRAL DNA, BURKITT'S
LYMPHOMA (0688)*
ETIOLOGY, HISTOLOGY, NASAL PAPILLOMA-
TOSIS (0373)
FBJ BONE TUMORS (0561)
FELINE LEUKEMIA, ANTIGEN, ISOLATION
(2312)
FELINE LEUKEMIA, CHARACTERIZATION
(1894)
FELINE LEUKEMIA, GROUP-SPECIFIC
ANTIGEN (1975), (1977)
FELINE LEUKEMIA, GROWTH IN HUMAN CELLS
(1895)
FELINE LEUKEMIA, INTERFERENCE, FELINE
CELLS (2311)

FELINE LEUKEMIA, PURIFICATION, CONCENTRATION (0164)
 FELINE LEUKEMIA, VIRAL ANTIGEN, VIRAL ANTIBODY (0163)
 FELINE LEUKEMIA, VIRAL RNA (1440)
 FELINE SARCOMA VIRUS, LYMPHOMA, TRANSMISSION (1441)
 FELINE SARCOMA, OSTEOSARCOMA, TRANSFORMATION, HUMAN (2298)
 FRIEND, ANTIGENIC TUMOR CELLS, RAT (0170)
 FRIEND, BACTERIAL ANTIGENS, REPLICATION OF VIRUS (1899)
 FRIEND, DEFECTIVE, SPLEEN, ANTISERA (1900)
 FRIEND, GRAFFI, LIVER, SERINE HYDROXY-METHYL TRANSFERASE, MOUSE (2317)
 FRIEND, IMMUNOLOGY, RAT (2411)
 FRIEND, LEUKEMIA, COMPLEMENT FIXATION, MOUSE (2456)
 FRIEND, LEUKEMIA, RADIATION, MAMMARY TUMOR, MOUSE (2348)
 FRIEND, LEUKEMIA, REGRESSION, MICE (2313)
 FRIEND, LEUKEMIA, REGRESSION, RESISTANCE, MOUSE (2412)
 FRIEND, NUCLEAR RNA SYNTHESIS (0601)
 FRIEND, POLIOVIRUS, ECHOVIRUS, LEUKEMIA, RNA (0572)
 FRIEND, RAUSCHER, ERYTHROCYTE, CARRIER (2322)
 FRIEND, SPLEEN, LEUKEMIA, RADIATION (1898)
 FRIEND, SPLEEN CELLS, IMMUNITY (1902)
 FRIEND, SPLEEN CELLS, PROTEIN SYNTHESIS (1032)
 FRIEND DISEASE, MYCOBACTERIUM BOVIS, IMMUNITY (1903)
 FRIEND LEUKEMIA, CELL COLONY-FORMING ABILITY (0603)
 FRIEND LEUKEMIA, DOUBLE STRANDED PENICILLIUM RNA, REGRESSION OF SPLENOMEGALY (1450)
 FRIEND LEUKEMIA, ERYTHROCYTES, OSMOTIC FRAGILITY (1033)
 FRIEND LEUKEMIA, GUAROA, ENHANCEMENT (0602)
 FRIEND LEUKEMIA, IMMUNOSUPPRESSION, MOUSE SPLEEN (1529)
 FRIEND LEUKEMIA, INHERITED SUSCEPTIBILITY, RESISTANT STRAIN (0169)
 FRIEND LEUKEMIA, INTERFERON, LACTATE DEHYDROGENASE (1454)
 FRIEND LEUKEMIA, MACROPHAGE MIGRATION, IMMUNITY (1534)
 FRIEND LEUKEMIA, MOUSE SPLEEN, ULTRASTRUCTURE OF ANTIBODY-FORMING CELLS (1535)
 FRIEND LEUKEMIA, PHAGOCYTOSIS, ANTIBODY FORMATION, 7,12-DIMETHYLBENZ(A)ANTHRACENE (1451)
 FRIEND LEUKEMIA, SPLEEN, LEUKEMIA (1022)
 FRIEND LEUKEMIA, SPLEEN, PARABIOSIS (1453)
 FRIEND LEUKEMIA, SPLEEN NUCLEOSIDE DEAMINASE ACTIVITY, MOUSE (1901)
 FRIEND LEUKEMIA, SURFACE ANTIGENS, RAT TUMORS (1533)

FROG, MUTATION, TEMPERATURE-SENSITIVITY (2301)
 FROG VIRUS 3, DNA REPLICATION, GAMMA RAYS (0522)
 FUJINAMI ROUS SARCOMA, CELL MEMBRANES MUCOPOLYSACCHARIDE LAYER (1948)
 GENITAL HERPES SIMPLEX, ANTIBODIES, HUMAN CERVIX CARCINOMA (0186)
 GENOME, TRANSFORMATION, DNA (2156)
 GRAFFI, MYELOGENOUS ELUKEMIA, ULTRASTRUCTURE, MOUSE (1040)
 GROSS, ANTITHYMOCYTE SERUM, LYMPHOMA INCIDENCE (1035)
 GROSS, BITTNER, INTERFERENCE, MOUSE (1928)
 GROSS, LEUKEMOGENESIS, CHROMOSOMES (1904)
 GROSS, LYMPHOMA, CELLULAR AND HUMORAL IMMUNE RESPONSE (1531)
 GROSS, MURINE LEUKEMIA, ANTIGEN (1523)
 GROSS, THYMUS GRAFT, LEUKEMIA SUSCEPTIBILITY (0172)
 GROSS LEUKEMIA, ANTIBODIES, GLOMERULONEPHRITIS, MOUSE (1034)
 GROSS LEUKEMIA, CYTOTOXIC ANTIBODY RESPONSE, LYMPHOMA (1520)
 GROSS LEUKEMIA, IMMUNIZATION OF PREGNANT MOTHERS, OFFSPRING IMMUNITY (1449)
 GROSS LEUKEMIA, IMMUNOFLOUORESCENT FOCUS ASSAY, ANTIBODY (1036)
 GROSS LEUKEMIA, IMMUNOLOGY, GENETICS (1970)
 GROSS LEUKEMIA, LYMPHOID LEUKEMIA, AKR-A CULTURE, MOUSE (0171)
 GROSS LEUKEMIA, X-IRRADIATION, SYNERGISM, LEUKEMOGENESIS (0604)
 GUINEA PIG, LEUKEMIA (1039)
 H-1, RNA SYNTHESIS INHIBITION, HUMAN KIDNEY CELLS (1099)
 HAMSTER-SPECIFIC C-TYPE, GROUP SPECIFIC ANTIGEN (0552)
 HAMSTER-SPECIFIC SARCOMA, ENVELOPE ANTIGEN RELATIONSHIPS (0551)
 HARVEY MURINE SARCOMA, INTERFERON, MORTALITY (0639)
 HARVEY MURINE SARCOMA, HELPER VIRUS FUNCTIONS, SPLENOMEGALY (1935)
 HEMAGGLUTININATING ADENOVIRUS, HEMAGGLUTINATION INHIBITOR, INTERACTION (0183)
 HEMAGGLUTINATION-INHIBITION, INFECTIVITY, RAT (0559)
 HERPES, ANTIGEN, BURKITT'S LYMPHOMA, MAN (2343)
 HERPES, GENITAL ORGANS, CANCER, REVIEW (1755)*
 HERPES, GIANT CELL FORMATION, RABBIT KIDNEY, COMPOUND 48/80, INHIBITOR (0188)
 HERPES, INFECTIVITY, CHEMICAL CONSTITUTION OF VIRUS, REVIEW (1759)
 HERPES, LUCKE ADENOCARCINOMA, FROG, TEMPERATURE (2340)
 HERPES, MAREK'S DISEASE, EPSTEIN-BARR, ANTIBODY, HUMAN SERA (1063)

HERPES, VIRAL ANTIGENS ON CELL
 MEMBRANES (1062)
 HERPES SAIMIRI, LYMPHOMA, MARMOSSET
 (2341)
 HERPES SAIMIRI, MORPHOLOGICAL CLASSI-
 FICATION (0619)
 HERPES SIMPLEX, ANTIBODY, PERSISTENCE,
 EARLE'S L CELLS, HUMAN (2334)
 HERPES SIMPLEX, ANTIGENS, CERVICAL
 CARCINOMA (0623)
 HERPES SIMPLEX, ARGINYL-TRNA, SERYL-
 TRNA, HUMAN EPIDERMAL CARCINOMA
 (1058)
 HERPES SIMPLEX, BURKITT'S LYMPHOMA
 CELLS, GROWTH (1923)
 HERPES SIMPLEX, CERVICAL EPITHELIUM,
 HUMAN (0620)
 HERPES SIMPLEX, CHROMOSOME, ABNORMAL-
 ITY (2342)
 HERPES SIMPLEX, CHROMOSOMES, L CELLS,
 HEP2 (1921)
 HERPES SIMPLEX, CYTOSINE ARABINOSIDE,
 CHROMOSOME CHANGES, HUMAN (2339)
 HERPES SIMPLEX, DNA SYNTHESIS, KB
 CELLS (2337)
 HERPES SIMPLEX, INFECTIVITY,
 7,12-DIMETHYLBENZ(A)ANTHRACENE
 (1463)
 HERPES SIMPLEX, LOCALIZATION OF VIRAL
 ANTIGENS, IMMUNOFERRITIN (1521)
 HERPES SIMPLEX, STRUCTURAL PROTEINS
 (1462)
 HERPES SIMPLEX, TEMPERATURE-SENSITIVE
 MUTANT (1060)
 HERPES SIMPLEX, THYMIDINE KINASE,
 ULTRAVIOLET (2336)
 HERPES SIMPLEX, ULTRASTRUCTURE,
 CLASSIFICATION (0002)
 HERPES SIMPLEX, VIRUS-LIKE PARTICLES,
 LEUKEMIC BONE MARROW CELLS (0149)
 HERPES SIMPLEX TYPE-2, ENVIRONMENTAL
 FACTOR, CERVIX (0187)
 HERPESLIKE VIRUS, GUINEA PIG,
 ISOLATION AND CHARACTERIZATION
 (1461)
 HERPES-TYPE, GUINEA PIG LEUKEMIA
 (1920)
 HERPES-TYPE, HUMAN PERIPHERAL BLOOD,
 LEUKEMIA (1925)
 HERPES-TYPE, INFECTION, LEUKOCYTE,
 GUINEA PIG (2335)
 HERPES-TYPE, KIDNEY TUMOR, FROG
 (2338)
 HERPES-TYPE, MAREK'S DISEASE (1031)
 HERPES-TYPE, MAREK'S DISEASE, CYTO-
 PATHIC AGENT (1030)
 HERPES-TYPE, NASOPHARYNGEAL CARCINOMA,
 BURKITT'S LYMPHOMA (1922)
 HERPES-TYPE, PROPAGATION, PROPERTIES,
 MAREK'S DISEASE (1029)
 HERPES-TYPE VIRUS, NASOPHARYNGEAL
 CARCINOMA, LYMPHOBLASTOID TRANS-
 FORMATION (0625)
 HERPESVIRUS, ENDOMETRIUM (0622)
 HERPESVIRUS HOMINIS, BURKITT'S
 LYMPHOMA, INHIBITION (2306)
 HERPESVIRUS HOMINIS, GENITAL INFECTION
 IN CEBUS MONKEY (1061)
 HERPESVIRUS HOMINIS, SARCOMA (0185)
 HERPESVIRUS HOMINIS, SEROLOGICAL
 TYPES, DIFFERENTIAL INFECTIVITY
 (1460)
 HERPESVIRUS SAIMIRI, ACUTE LYMPHOCYTIC
 LEUKEMIA, MALIGNANT LYMPHOMA (1464)
 HERPESVIRUS SAIMIRI, INTERFERON,
 POLY I.C (1918)
 HERPESVIRUS SAIMIRI, MALIGNANT
 LYMPHOMA, MONKEYS (1917)
 HERPESVIRUS SAIMIRI, PLAQUE FORMATION
 (1919)
 HERPESVIRUS SAIMIRI, RETICULOPRO-
 LIFERATIVE DISEASE, RINGTAIL
 CINNAMON MONKEY (1059)
 HERPESVIRUS 2, ANTIBODIES, INVASIVE
 CERVICAL CARCINOMA (0624)
 HERPESVIRUS 2, CERVICAL
 CARCINOMA, ANTIBODIES (1924)
 HERPESVIRUS OF TURKEY, MAREK'S DISEASE
 MORPHOLOGY OF TRANSFORMED CELLS
 (1465)
 HUMAN ADENO TYPE 12, SARCOMA, ANTIGEN,
 HAMSTER (1050)
 HUMAN ADENOVIRUS TYPE 12, CHICKEN
 LEUKOCYTES, INTERFERON PRODUCTION
 (1045)
 HUMAN LYMPHOBLASTS, EPSTEIN-BARR,
 INFECTIVITY AND CYTOPATHOLOGY (1023)
 HUMAN LEUKEMIA, REVERSE TRANSCRIPTASE
 (0352)
 HUMAN LEUKEMIC CELLS, INDUCTION OF
 LEUKEMIA, MONKEYS (1867)
 HUMAN NASOPHARYNGEAL (1423)
 HUMAN SARCOMAS, ANTISARCOMA ANTIBODIES
 (1880)
 HYBRID, SV40, ADENOVIRUS 7, TRANS-
 FORMATION (1509)
 INFLUENZA, LUNG CANCER, MICE, CELL
 METAPLASIA (0564)
 INTRACISTERNAL A-PARTICLES, MOUSE
 NEOPLASTIC TISSUE (1422)
 ISOLATE, MAMMARY CARCINOMA, LUNG,
 LEUKOCYTES, MONKEY (1420)
 ISOLATION OF NEW VIRUS, AVIAN TUMOR
 VIRUSES, CHICK EMBRYO FACTOR (1086)
 KILHAM RAT, DNA (2399)*
 KILHAM RAT, DNA POLYMERASE (2300)
 KILHAM RAT, STRUCTURAL PROTEINS
 (1071)
 KIRSTEN MURINE SARCOMA, RAUSCHER
 MURINE LEUKEMIA, GENETIC ALTERATION,
 HUMAN CELL CULTURE (2352)
 LACTIC DEHYDROGENASE-ELEVATING VIRUS,
 POTENTIATION OF TUMORIGENICITY,
 MURINE SARCOMA VIRUS (1933)
 LACTIC DEHYDROGENASE PASSENGER,
 RAUSCHER LEUKEMIA, THYMIC LYMPHOCYTE
 SPLEEN (0609)
 LARGE AND SMALL PLAQUE VARIANTS,
 VIRULENCE, HERPES (1057)
 LATENT ONCOGENIC, PRECIPITATING FACTOR
 LEUKEMIA (0351)
 LEUKEMIA, ACTIVATION, SPECIES
 SPECIFICITY, DOG MOUSE (2319)
 LEUKEMIA, ANTIGENICITY, HUMAN CELLS,
 ANIMAL CELLS (2295)
 LEUKEMIA, ANTIGENS, DETECTION (2413)

LEUKEMIA, COMPLEMENT BINDING, ANTIGENS
 RABBIT, MAN (0711)
 LEUKEMIA, MAN, REVIEW (0867)*
 LEUKEMIA, MOUSE, SPLEEN, WHOLE BODY
 IRRADIATION (0592)
 LEUKEMIA ANTIGEN, SUPPRESSION OF TUMOR
 GROWTH, IMMUNE LYMPHOCYTES (1969)
 LEUKEMOGENIC, GUINEA PIG LEUKEMIA
 (1871)
 LEUKEMOGENIC, SARCOMAGENIC, ULTRA-
 STRUCTURE (1866)
 LEUKOCYTIC LEUKEMIA, HUMAN, EVIDENCE,
 MORPHOLOGY (1418)
 LEUKOVIRUS, HUMAN, HEMATOPOIETIC
 (0571)
 LONG-TERM CELL CULTURE, SUSCEPTI-
 BILITY TO VIRUS, RAT (1412)
 LUCKE ADENOCARCINOMA FROG HERPESVIRUS,
 BURKITT'S LYMPHOMA, VIRAL DNA
 SENSITIVITIES (0621)
 LYMPHOSARCOMA AND LEUKEMIA VIRUS
 PARTICLES, MORPHOLOGY AND DISTRIBUTION
 (0550)
 MAMMARY TUMOR, ALLOGRAFT SURVIVAL,
 IMMUNOLOGIC DEFICIENCY (1530)
 MAMMARY TUMOR, AMINOPEPTIDASE ACTIVITY
 (1470)
 MAMMARY TUMOR, ANTIBODIES, MICE (2453)
 MAMMARY TUMOR, ANTIGEN, MURINE (2160)
 MAMMARY TUMOR, ANTIGENICITY, MICE
 (2349)
 MAMMARY TUMOR, BRAIN AND LIVER
 EXTRACTS, GR STRAIN MICE (0629)
 MAMMARY TUMOR, CELL FUSION, IMMUNO-
 FLUORESCENCE STUDY, MURINE (1926)
 MAMMARY TUMOR, COMMON ANTIGENICITY IN
 MOUSE TUMORS (1536)
 MAMMARY TUMOR, ERYTHROCYTES, DNA,
 MOUSE (2345)
 MAMMARY TUMOR, FOSTER-NURSED C3HFB AND
 C3HEB MICE, TRANSMISSION (0193)
 MAMMARY TUMOR, IMMUNOGENICITY, MICE
 (2402)
 MAMMARY TUMOR, MAMMARY CARCINOMA
 (0633)
 MAMMARY TUMOR, MILK (1067)
 MAMMARY TUMOR, MILK TRANSMISSION IN
 MICE, GENETIC SUSCEPTIBILITY TRANS-
 MISSION (0631)
 MAMMARY TUMOR, MOUSE INBRED STRAINS,
 TUMOR INCIDENCE (1471)
 MAMMARY TUMOR, NODULE OUTGROWTH LINE D
 BABL/C, METHYLCHOLANTHRENE (0076)
 MAMMARY TUMOR, RNA, ANTIGEN CROSS-
 REACTION (1927)
 MAMMARY TUMOR, THYMECTOMY, SPLENECTOMY
 (2344)
 MAMMARY TUMOR AGENT, ANTIGEN, GLYCO-
 PROTEIN (0191)
 MAREK'S DISEASE, AGENT, CHICKEN EMBRYO
 (1915)
 MAREK'S DISEASE, CHICKEN FEATHER
 FOLLICLES (1916)
 MAREK'S DISEASE, DNA (2310)
 MAREK'S DISEASE, HERPES, ANTIGEN,
 INFECTIVITY (0157)
 MAREK'S DISEASE, HERPES, IMMUNE
 RESPONSE, CHICKEN (1468)

MAREK'S DISEASE, HERPESVIRUS, TURKEYS,
 PATHOGENICITY (1467)
 MAREK'S DISEASE, HERPESVIRUS, VIRAL
 ANTIGENS IN CHICKEN FEATHER
 FOLLICLES (1965)
 MAREK'S DISEASE, HERPESVIRUS CAL1,
 PLAQUE TYPE, TISSUE CULTURE (0159)
 MAREK'S DISEASE, RNA, TRANSFER,
 METHYLATION (2309)
 MAREK'S DISEASE, SENDAI (0581)
 MOLONEY, CELL CULTURES, MITOTIC
 RATES, ANTIGENS (1473)
 MOLONEY, OSTEOSARCOMA, RAT (0637)
 MOLONEY, RAUSCHER, IMMUNITY, MOUSE
 (0635)
 MOLONEY LEUKEMIA, C-TYPE PARTICLES
 (1447)
 MOLONEY LEUKEMIA, JLSV-9 CELLS, CELL
 SENSITIVITY (1445)
 MOLONEY LEUKEMIA, LYMPHOMA, MURINE
 (1077)
 MOLONEY LEUKEMIA, STREPTOVIRICIN,
 RNA DEPENDENT DNA POLYMERASE
 INHIBITION (1444)
 MOLONEY LEUKEMIA, TRANSMISSION,
 CHROMOSOME (1905)
 MOLONEY LEUKEMIA, TUMORIGENESIS, SOLID
 LYMPHATIC TUMORS, MICE (1443)
 MOLONEY LEUKEMOGENIC, PLASMODIUM
 BERGHEI YOELII, LYMPHOMA (0600)
 MOLONEY LEUKEMOGENIC, PREDNISOLONE,
 THYMUS (0173)
 MOLONEY MURINE SARCOMA, HARVEY MURINE
 SARCOMA, INDUCTION OF BONE TUMORS
 (1938)
 MOLONEY MURINE SARCOMA, HELPER,
 ISOLATION, RAT (2353)
 MOLONEY MURINE SARCOMA, RECOVERY FROM
 BOVINE MILK (1474)
 MOLONEY MURINE SARCOMA, RODENT SARCOMA
 (1930)
 MOLONEY MURINE SARCOMA, TRANSFORMATION
 IN VITRO, KIDNEY CELL CULTURE (1937)
 MOLONEY SARCOMA, RESCUE, VIRUS CARRIER
 CELL LINE, HAMSTER TUMOR CELL (1070)
 MOUSE MAMMARY TUMOR, GENETIC TRANS-
 MISSION (0627)
 MOUSE MAMMARY TUMOR, INOCULATION AGE,
 MILK ANTIGEN ASSAY (0194)
 MOUSE MAMMARY TUMOR, ISOLATION,
 HUMAN MILK (1419)
 MURINE C-TYPE RNA, GROUP-SPECIFIC
 ANTIGEN (0597)
 MURINE LEUKEMIA, ANTIGEN, LOW-LEUKEMIA
 STRAIN MICE (0596)
 MURINE LEUKEMIA, CELL FUSION (2315)
 MURINE LEUKEMIA, COMPLEMENT FIXATION,
 HEMAGGLUTINATION REACTION (1909)
 MURINE LEUKEMIA, CROSS IMMUNIZATION,
 INTERFEROGENESIS (0595)
 MURINE LEUKEMIA, DNA, SINGLE- OR
 DOUBLE-STRANDED (1446)
 MURINE LEUKEMIA, DNA POLYMERASE,
 MURINE CELL (2320)
 MURINE LEUKEMIA, GROUP-SPECIFIC ANTI-
 GEN (0598)
 MURINE LEUKEMIA, HEMOGLOBIN SYNTHESIS
 DBA/2J (1897)

MURINE LEUKEMIA, INTRACISTERNAL VIRAL PARTICLES (1442)
 MURINE LEUKEMIA, LYMPHOCYTIC LEUKEMIA, ANTILYMPHOCYTE SERUM (1543)
 MURINE LEUKEMIA, MURINE SARCOMA, INACTIVATION, ULTRAVIOLET (1452)
 MURINE LEUKEMIA, POLYINOSINIC-POLYCYTIDYLIC ACID, INTERFERON, EMBRYO CELLS (0953)
 MURINE LEUKEMIA, PLAQUE ASSAY TECHNIQUES (1115)*
 MURINE LEUKEMIA, RESCUE OF PSEUDOTYPE SARCOMA, NEW ZEALAND BLACK MICE (0606)
 MURINE LEUKEMIA, THYMIC LYMPHOMA, ALKALINE PHOSPHATASE, RAT (0590)
 MURINE LEUKEMIA, THYMUS-INDEPENDENT LYMPHOSARCOMA, PREDNISOLINE (0167)
 MURINE MAMMARY TUMOR, HUMAN BREAST CANCER, NEUTRALIZATION (1929)
 MURINE MAMMARY TUMOR, RNA, FLUORESCENCE MICROSCOPY (1469)
 MURINE MYELOPROLIFERATIVE, LEUKEMIC MOUSE CELL CULTURE (0166)
 MURINE SARCOMA, BALB/3T3 CULTURE, MURINE LEUKEMIA VIRUS (0199)
 MURINE SARCOMA, CELL CYCLE, ULTRAVIOLET IRRADIATION (0198)
 MURINE SARCOMA, CELL MULTIPLICATION (0636)
 MURINE SARCOMA, CELL TRANSFORMATION, MULTIPLICATION (1068)
 MURINE SARCOMA, DEFECTIVENESS (1936)
 MURINE SARCOMA, DIETHYLAMINOETHYL-DEXTRAN, TUMOR ENHANCEMENT (2351)
 MURINE SARCOMA, DNA POLYMERASE, RNA (0634)
 MURINE SARCOMA, FELINE LEUKEMIA, ALTERATION IN CULTURE (1934)
 MURINE SARCOMA, GROUP-SPECIFIC ANTIGEN (1476)
 MURINE SARCOMA, LEUKEMIA, RNA (1076)
 MURINE SARCOMA, LEUKEMIA HELPER VIRUS (0195)
 MURINE SARCOMA (MOLONEY), GUAROA, ENHANCEMENT, MICE (1069)
 MURINE SARCOMA, MURINE LEUKEMIA, NONPRODUCER VIRAL CLONES (0638)
 MURINE SARCOMA, MOUSE, HAMSTER, CAT, ANTIGEN (2356)
 MURINE SARCOMA, PATHOLOGY, IMMUNOGENICITY (1472)
 MURINE SARCOMA, PLASMA VARIANT, SPLENOMEGALY (0196)
 MURINE SARCOMA, REVIEW (2169)*
 MURINE SARCOMA, RNA (2355)
 MURINE SARCOMA, THYMIC EXTRACT, RESISTANCE TO TUMOR GROWTH (0197)
 MURINE SARCOMA, TUMOR REGRESSION, NEW ZEALAND MICE (1932)
 MURINE SARCOMA, VIRAL ANTIGENICITY, (2458)
 MYELOBLASTOSIS, AVIAN, ANTIGEN (1967)
 MYELOCYTOMATOSIS, DNA POLYMERASE, INFECTED CHICK CELLS (1893)
 MYELOID LEUKEMIA, STAPHYLOCOCCUS, CHICK (1889)

MYXOVIRUS INFECTION, X-IRRADIATION, CHROMOSOME ABERRATIONS (1002)
 4-NITROQUINOLINE-1-OXIDE, DNA REPAIR SYNTHESIS (1356)
 ONCOGENESIS IN MAN, MICROEPIDEMICS (1267)
 ONCOGENIC, ANIMAL CELLS, TRANSFORMATION (2164)*
 ONCOGENIC, DNA POLYMERASE, RNA HYBRID (0142)
 ONCOGENIC, DNA-DNA POLYMERASE DOUBLE STRAND TEMPLATE (0141)
 ONCOGENIC, ENDOGENOUS INTERFERON, REVIEW (0021)*
 ONCOGENIC, POLYMERASE, NUCLEIC ACID (0553)
 ONCOGENIC, PRIMATE, LEUKEMIA, REVIEW (0003)
 ONCOGENIC, RNA, DNA, SEQUENCES, HYBRIDIZATION (1438)
 ONCOGENIC RNA, BIOLOGICAL PROPERTIES, BIOCHEMICAL PROPERTIES (0837)
 ONCOGENIC RNA, CELL TRANSFORMATION, REVIEW (0020)*
 ONCOGENICITY, HERPES GROUP (1752)*
 PAPILLOMA, WART, KERATIC PAPILLOMA, EPIDERMODYSPLASIA VERRUCIFORMIS (1516)*
 PAPOVA, HAMSTER PAPILLOMAS, LYMPHOMA (1956)
 PAPOVA, THYMUS, LIVER, LEUKEMIA (0672)
 PARA-ADENOVIRUS 7, TUMOR CELL POLYMORPHISM, IMMUNOLOGY, HAMSTER (2326)
 PARAMYXOVIRUS, SARCOMA, HUMAN, ULTRASTRUCTURE (2558)
 PARTICLES, ANTIGEN, MAMMARY TUMOR, MOUSE (2347)
 PARTICLES, ELECTRON MICROSCOPIC STUDY, MAMMARY CARCINOMA (0146)
 PARTICLES, HUMAN LEUKEMIA AND LYMPHOMA (0569)
 PARTICLES, MEDIASTINAL LYMPHOMA, LUNG EPITHELIOMA, URETHAN, GERM-FREE MOUSE (0494)
 PARTICLES, OVINE PULMONARY ADENOMAS, ULTRASTRUCTURE OF TUMORS (1411)
 PARTICLES, PLASMA CELL GRANULOMA, MINERAL OIL (0396)
 PARTICLES, RAT MAMMARY ADENOCARCINOMA (0630)
 PARTICLES, SPONTANEOUS LYMPHOMAS, RADIATION, HAMSTERS (1868)
 PARTICLES, THYMUS, EPIDIDYMISS, HEMATOMOETIC ORGANS, MOUSE (0632)
 PARTICLES IN GUINEA PIG LEUKEMIA, TRANSMISSION (1865)
 PASSAGE IN VITRO OF SV40, POTENTIATION OF TUMORIGENICITY (1093)
 PARVOVIRUS H-1, SV40, THYMIDINE KINASE, DNA SYNTHESIS (0210)
 POLYKARYOCYTOSIS, CELL FUSION (1019)
 POLYOMA, ADENOCARCINOMA, TUMOR ANTIGEN (1515)
 POLYOMA, AGGLUTININ, CONTACT INHIBITION, CONCAVALIN A (0679)
 POLYOMA, ANTIGENIC DIFFERENCES, IMMUNOCHEMICAL ANALYSIS (1107)

POLYOMA, ARGININE DEPRIVATION, MOUSE EMBRYO CULTURES (1112)
 POLYOMA, AT-TYPE FIBROSARCOMA, GC-TYPE ADENOCARCINOMA (0220)
 POLYOMA, BHK, GLYCOSYLTRANSFERASE ACTIVITY (1958)
 POLYOMA, BHK 21 (1959)
 POLYOMA, BHK 21 HAMSTER ALL, DNA SYNTHESIS, SERUM (0216)
 POLYOMA, CELL PROLIFERATION, MURINE (2389)
 POLYOMA, CELL TRANSFORMATION, VIRUS GENERATION IN VITRO (0667)
 POLYOMA, 7,12-DIMETHYLBENZ(A)ANTHRACENE, 3-METHYLCHOLANTHRENE, CELL GROWTH, IN VITRO, HAMSTER (2194)
 POLYOMA, DNA, THERMOSENSITIVE MUTANT (1109)
 POLYOMA, DNA SYNTHESIS, CYCLOHEXIMIDE, MOUSE EMBRYO CELL (1110)
 POLYOMA, DNA SYNTHESIS, MITOCHONDRIA (1513)
 POLYOMA, DNA SYNTHESIS, MOUSE EMBRYO CELL (1106)
 POLYOMA, FIBROBLAST SUSPENSION, SURFACE INTERACTIONS (2387)
 POLYOMA, GLYCOPROTEIN SYNTHESIS, HAMSTER KIDNEY CELLS (1114)
 POLYOMA, HAMSTER, INTERFERON INDUCTION (1519)
 POLYOMA, HAMSTER KIDNEY CELL CULTURE, ENDONUCLEASE (0674)
 POLYOMA, HAMSTERS, TRANSFORMED CELLS (1421)
 POLYOMA, HOST RANGE MUTANTS (0681)
 POLYOMA, HYBRIDIZATION, MOUSE, HAMSTER (2382)
 POLYOMA, IMMUNE RESPONSE TO TUMORS (1113)
 POLYOMA, IMMUNITY, ANTIGENS, RAT (2454)
 POLYOMA, IMMUNITY, BACTERIOPHAGE, BHK (2388)
 POLYOMA, IMMUNOSUPPRESSION, RESTORATION OF IMMUNOCOMPETENCE (1117)
 POLYOMA, INHIBITION OF ONCOGENESIS, POLYRIBOINOSINIC-POLYRIBOCYTIDYLIC ACID (0685)
 POLYOMA, MOUSE EMBRYO FIBROBLAST, VIRUS-DNA COMPLEX FORMATION (1111)
 POLYOMA, MOUSE KIDNEY CELL CULTURE, DNA SYNTHESIS, T-ANTIGEN (0676)
 POLYOMA, M-RNA SYNTHESIS, MOUSE EMBRYO CELLS (0218)
 POLYOMA, MUTANT, TEMPERATURE SENSITIVITY, DNA SYNTHESIS (2384)
 POLYOMA, NON-TRANSFORMING MUTANT, CELL MEMBRANE AGGLUTINATION (0680)
 POLYOMA, PHENOTYPE (2385)
 POLYOMA, RECOVERY, METHODOLOGY (2392)*
 POLYOMA, RNA SYNTHESIS, MOUSE (2400)*
 POLYOMA, ROUS SARCOMA, SENDAI, EMBRYONIC HUMAN FIBROBLAST (0675)
 POLYOMA, ROUS TUMOR, IMMUNITY, RAT (2455)
 POLYOMA, SALIVARY GLAND TUMOR (0219)
 POLYOMA, SARCOMA, PROTEIN SYNTHESIS (1108)

POLYOMA, SPLENIC LYMPHOID TUMORS, ANTITHYMOCYTE SERUM (0682)
 POLYOMA, SUBMAXILLARY GLAND, CHROMOSOME (1512)
 POLYOMA, SV40, ADENOVIRUS, TRANSFORMED-CELL SURFACE MEMBRANE, AGGLUTINATION (0708)
 POLYOMA, SV40, PURIFICATION BY POLYETHYLENE GLYCOL PRECIPITATION (0684)
 POLYOMA, T ANTIGEN PRODUCTION (1510)
 POLYOMA, TEMPERATURE-SENSITIVE MUTANT POLYOMA VIRUS, 3T3 CULTURE, BALB/C-3T3 CULTURE (0673)
 POLYOMA, TEMPERATURE-SENSITIVE POLYOMA MUTANT, INTERFERON, DNA, 3T3 CELL CULTURE (0678)
 POLYOMA, 3T3 MOUSE CELL, BHK21 HAMSTER CELL, GROWTH REGULATION (0350)
 POLYOMA, TRANSFER RNA, METHYLATION (0217)
 POLYOMA, TRANSFORMATION, INTERFERON, BHK (2390)
 POLYOMA, TRANSFORMED CELL, TUMOR, HAMSTER (2383)
 POLYOMA, TRANSFORMED CELL LINES, HAMSTER (0215)
 POLYOMA, TRANSFORMED CELLS, GLYCOPOLYMER (1957)
 POLYOMA, TRANSFORMED MOUSE CELLS, IMMUNE SERUM (1104)
 POLYOMA, TRNA, RAT (1962)
 POLYOMA, TUMOR CELL CLONES, ANTIGENS, MOUSE (2391)
 POLYOMA, U.V. IRRADIATION, TUMOR EXTRACT, IMMUNOTHERAPY, HAMSTER (0241)*
 POLYOMA, VIRUS SYNTHESIS IN VITRO, PHLEOMYCIN (1511)
 POLYOMA PSEUDOVIRUS, UNCOATING, MOUSE EMBRYO CELLS (0683)
 POLYOMA TUMORS, ANTIGEN, SHEEP ERYTHROCYTES, HAMSTER CELLS (2437)
 POLYOMA VIRUS, HAMSTER CELLS, GLYCOLIPIDS, PHOSPHOLIPIDS, HEMATOSIDES, CERAMIDES (1514)
 PROTEIN SYNTHESIS, NUCLEIC ACID, PAPOVA (1426)
 PSEUDOTYPE SARCOMA, HAMSTER, GLUCOSE UPTAKE (2354)
 RADIATION, IMMUNIZATION, LEUKEMIA (1968)
 RADIATION LEUKEMIA, HOST FACTORS, MICE (2434)
 RAUSCHER, ANTIBODIES, MOUSE (1448)
 RAUSCHER, ANTIGEN SUBUNITS, HEMAGGLUTINATION-INHIBITION ASSAY (2409)
 RAUSCHER, 7,12-DIMETHYLBENZ(A)ANTHRACENE, TRANSFORMATION (1326)
 RAUSCHER, FREUND ADJUVANT, MOUSE (2323)
 RAUSCHER, POLYRIBOSOME, SPLEEN, MOUSE (0607)
 RAUSCHER, RNA, SPLEEN, MOUSE (1038)
 RAUSCHER LEUKEMIA, ASPARTYL TRANS-CARBAMYLASE, BLOOD, MOUSE (2321)

RAUSCHER LEUKEMIA, CHANGES IN ENZYME ACTIVITY, LEUKEMIA (1907)
 RAUSCHER LEUKEMIA, DECREASED LEUKEMOGENICITY IN CULTURE (1910)
 RAUSCHER LEUKEMIA, ENTRY INTO CELL, MOUSE (2318)
 RAUSCHER LEUKEMIA, HIGH AND LOW LEUKEMOGENIC VIRAL VARIANTS (1908)
 RAUSCHER LEUKEMIA, MAGNESIUM ACETATE, MANGANESE ACETATE (1037)
 RAUSCHER LEUKEMIA, SPLENOMEGALY, SHEEP ERYTHROCYTE IMMUNIZATION (0174)
 INHIBITION (1463)
 ROUS SARCOMA, CHICK EMBRYO CELLS, SUGAR TRANSPORT (0204)
 ROUS SARCOMA, CHICK EMBRYO FIBROBLASTS RIFAMPICIN (1944)
 ROUS SARCOMA, DEFECTIVE, DNA POLYMERASE (2398)*
 ROUS SARCOMA, DNA, EXONUCLEASE, LIGASE (2368)
 ROUS SARCOMA, DNA ISOLATION (0203)
 ROUS SARCOMA, DNA POLYMERASE (1941)
 ROUS SARCOMA, DNA POLYMERASE, CHICKEN CELL (2358)
 ROUS SARCOMA, DNA SYNTHESIS, IN VITRO (2357)
 ROUS SARCOMA, EMBRYONIC TISSUE CULTURES, GRAFT (0654)
 ROUS SARCOMA, GLYCOLIPID, TRANSFORMATION (2359)
 ROUS SARCOMA, IMMUNIZATION, CHICKEN (2436)
 ROUS SARCOMA, IMMUNOSUPPRESSION, HAMSTER (2360)
 ROUS SARCOMA, INHIBITION OF FOCUS-FORMATION, METHOTREXATE, L-ASPARAGINASE (1480)
 ROUS SARCOMA, KARYOTYPES OF TUMOR CELL (0591)
 ROUS SARCOMA, LOW MOLECULAR WEIGHT RNA, 4S (0646)
 ROUS SARCOMA, METASTASIS, CHROMOSOME, RAT (1084)
 ROUS SARCOMA, METASTASIS, NEOPLASM, MARMOSET (0200)
 ROUS SARCOMA, PARTICLES, HAMSTERS, CHICK CELLS, MAMMALIAN CELLS (1481)
 ROUS SARCOMA, POLYMERASE (0648)
 ROUS SARCOMA, POLYMERASE, ENDONUCLEASE RNA, DNA (0647)
 ROUS SARCOMA, POLYMERASE, RNA, DNA (0651)
 ROUS SARCOMA, POLYOMA, KARYOTYPE, HAMSTER CELLS (2364)
 ROUS SARCOMA, POLYOMA, SARCOMA 180, PROLIFERATION (0814)
 ROUS SARCOMA, PROLIFERATION, CHICKEN EMBRYO CELLS (1082), (1083)
 ROUS SARCOMA, PROTEIN COMPONENTS (1482)
 ROUS SARCOMA, RABIES VIRUS VACCINE, CHICKEN (0652)
 ROUS SARCOMA, REPLICATION, NUCLEIC ACID INTERMEDIATES (2362)
 ROUS SARCOMA, RNA, CHICKEN, MOUSE (2365)
 RAUSCHER LEUKEMIA, TUMORIGENIC MOUSE

CELLS, DECREASED TUMORIGENICITY (1906)
 RAUSCHER MURINE LEUKEMIA, LEUKEMOGENESIS, AEROSOL EXPOSURE (0608)
 RAUSCHER MURINE LEUKEMIA, ULTRA-STRUCTURE, DNA (0176)
 REOVIRUS 3, LYMPHOMA, MURINE (2316)
 RETICULUM CELL SARCOMA, MOUSE (1075)
 RNA, DNA (2299)
 RNA, DNA, REVIEW (0381)*
 RNA, RENAL TISSUE, CHICKS, NEPHRO-BLASTOMA (1436)
 RNA-METHYLATING ENZYMES, E.COLI (2304)
 RNA, RNA-DEPENDENT, DNA POLYMERASE, ONCOGENIC (0557)
 RNA TUMOR, GROUP-SPECIFIC ANTIGEN (0562)
 RNA TUMOR VIRUS, SEROLOGY, HAMSTER (2395)*
 RNA TUMOR VIRUSES, VIRION RNA SYNTHESIS (1940)
 RNA-TYPE, ISOLATION, MONKEY MAMMARY CARCINOMA (0626)
 ROUS, DEFECTIVE STRAIN, HELPER, CHICKEN EMBRYO (1947)
 ROUS, GENOME SUBUNITS, TRANSFORMATION, CHICK EMBRYO FIBROBLASTS (1078)
 ROUS, MURINE SARCOMA, CHICK EMBRYO, MOUSE (2367)
 ROUS, POLYOMA, CELL TRANSFORMATION STAGES, HAMSTER (0556)
 ROUS, POLYOMA, CELL TRANSFORMATION, ULTRASTRUCTURE, AMP (1079)
 ROUS SARCOMA, ANTIGEN, CHICK CELLS, IMMUNOCHEMICAL CHARACTERIZATION (1527)
 ROUS SARCOMA, ANTIGENS, "VIRUS FREE" TUMORS (0655)
 ROUS SARCOMA, ANTI-LYMPHOCYTE SERUM, QUAIL (2446)
 ROUS SARCOMA, ASCITIC SARCOMA, NUCLEIC ACID, MOUSE CELL (1080)
 ROUS SARCOMA, AVIAN LEUKOSIS, CHICK EMBRYO CELL CULTURE, DNA SYNTHESIS (0566)
 ROUS SARCOMA, AVIAN LEUKOSIS IN PIGEONS, COMPLEMENT FIXING ANTIGEN (1966)
 ROUS SARCOMA, AVIAN MYELOBLASTOSIS, DNA POLYMERASE (1081)
 ROUS SARCOMA, LACTERIA (1946)
 ROUS SARCOMA, CELL SURFACE GLYCOPROTEINS (1939)
 ROUS SARCOMA, CHICK EMBRYO, CONTACT
 ROUS SARCOMA, RNA SYNTHESIS, BROMO-DEOXYURIDINE (0645)
 ROUS SARCOMA, ROUS ASSOCIATED, VIRION CORE ANALYSIS (0206)
 ROUS SARCOMA, SARCOMA VOLE (0642)
 ROUS SARCOMA, 7S VIRAL RNA (1088)
 ROUS SARCOMA, SONIC DISRUPTION, OVERGROWTH STIMULATING ACTIVITY (0644)
 ROUS SARCOMA, TRANSFORMED HAMSTER CELLS, VIRAL GENOME (1486)
 ROUS SARCOMA, TRANSFORMED STATE, TEMPERATURE SENSITIVE MUTANT (0205)

ROUS SARCOMA, TRANSFORMATION,
 REVERSION, HAMSTER CELLS (2361)
 ROUS SARCOMA, TUMOR RECURRENCE (0650)
 ROUS SARCOMA, TUMOR SPECIFIC ANTIGEN,
 MOUSE (0653)
 ROUS SARCOMA, ULTRASTRUCTURE OF CANINE
 GLIOMAS (1484)
 ROUS SARCOMA, URIDINE METABOLISM,
 CHICK CHORIOALLANTOIC MEMBRANE
 (0643)
 ROUS SARCOMA, UV ACTIVATION, HELPER
 (1479)
 ROUS SARCOMA, VARIANT STRAIN,
 TUMORIGENICITY FOR MAMMALS (1087)
 ROUS SARCOMA, VESICULAR STOMATITIS,
 SMALLPOX VACCINE (0560)
 ROUS SARCOMA, VIRUS-SPECIFIC RNA
 (1487)
 ROUS SARCOMA MUTANT, FUSIFORM CELL
 TRANSFORMATION (0649)
 ROUS SARCOMA TYPE 0, DILUTION,
 PROGENY, QUAIL (2366)
 ROUS SARCOMA VIRUS COAT ANTIGEN,
 HETEROKARYOTIC CELLS, VIROGENIC CELL
 FUSION (0201)
 ROWSON-PARR, INDUCTION OF LYMPHOMA,
 MICE (0610)
 SARCOMA, ANTIBODY, HUMAN (0147)
 SARCOMA, LEUKEMIA, TRANSFORMATION,
 MOUSE, RAT (2350)
 SARCOMA-LEUKEMIA VIRUS, VIRAL RNA-DNA
 HYBRID MOLECULE, DNA POLYMERASE
 TEMPLATE (0143)
 SARCOMA 180, ANTIGEN (1995)
 SCHMIDT-RUPPIN ROUS, SARCOMA, THYMUS,
 CHICKEN (0656)
 SENDAI, HAMSTER, CHICK EMBRYO, M-RNA
 (0207)
 SHOPE, VX7 TYPE CARCINOMA, PAPILLOMAS,
 NUCLEIC ACID (1074)
 SHOPE FIBROMA, COWPOX, CELLULAR DNA
 SYNTHESIS, INHIBITION (2380)
 SHOPE FIBROMA, CYTOCIDAL VIRUS, RABBIT
 (2379)
 SHOPE FIBROMA, DNA, RK 13, LACK OF
 HOMOLOGY (1949)
 SHOPE FIBROMA, FOCUS FORMATION,
 NUCLEIC ACID SYNTHESIS (0657)
 SHOPE PAPILLOMA, ANTIGENICITY (0658)
 SHOPE PAPILLOMA, ENZYME, RABBIT (2381)
 SHOPE PAPILLOMA, EPIDERMAL PAPILLOMAS
 (1522)
 SIMIAN ADENOVIRUS, DNA, DENSITY (2296)
 SIMIAN ADENOVIRUS 7, 7,12-DIMETHYL-
 BENZO(A)ANTHRACENE, TUMOR TRANSPLANT
 IMMUNITY (1982)
 SIMIAN ADENOVIRUS 7, HAMSTER CELLS
 (2324)
 SIMIAN ADENOVIRUS 7, PROPERTIES OF
 VIRUS POPULATION (1457)
 SKIN-HETEROGENIZING, SARCOMA K-237,
 MICE (0144)
 SKIN HETEROGENIZING, STRAIN SPECIFIC
 VIRUS, GENETIC TRAIT (0145)
 SMALLPOX VACCINATION, FIBROSARCOMA
 (1416)
 SNYDER-THEILEN FELINE SARCOMA, FILTER-
 ABLE AGENT, HUMAN CELL CULTURES (1073)

SPECIES-SPECIFIC VIRUS, POLIOVIRUS,
 SV40, ADENOVIRUS, POLYOMA (1507)
 SV40, ADENOVIRUS 2, HYBRID, VIRAL DNA
 (2332)
 SV40, ADENOVIRUS 12, ORNITHINE,
 LEUCINE POLYMER, AGGREGATION OF
 TRANSFORMED CELLS (0661)
 SV40, ADENOVIRUS 12, ULTRAVIOLET
 IRRADIATION, BRAIN (1489)
 SV40, ADENOVIRUS HYBRID, TRANSFORMA-
 TION, ANTIGEN (0615)
 SV40, ANTIBODY, LABORATORY MONKEY
 HANDLERS (1524)
 SV40, ANTIBODY, PREGNANT HAMSTERS
 (0213)
 SV40, ANTI-MOUSE EGG ANTIGEN, CYTO-
 TOXICITY (0669)
 SV40, BOVINE, KIDNEY, HAMSTER, LUNG,
 CHROMOSOMES (1491)
 SV40, C-TYPE POLYPEPTIDE (1497)
 SV40, CELL ASSOCIATION, RECOVERY
 (1955)
 SV40, CELL HYBRIDS, UV RADIATION,
 IN VITRO (1517)*
 SV40, CELL MEMBRANE, ANTIGEN, KIDNEY
 (2447)
 SV40, CELL TRANSFORMATION, TUMOR-
 ANTIGEN PRODUCTION (0349)
 SV40, CYCLOHEXIMIDE, DNA REPLICATION,
 (1504)
 SV40, DEFECTIVE, ANTIGENIC RESPONSE
 (1100)
 SV40, DNA, TRANSFORMATION SUSCEPTI-
 BILITY (0659)
 SV40, DNA FORMS, CYCLOHEXIMIDE (1503)
 SV40, DNA OLIGOMERS (2378)
 SV40, DNA PROPERTIES, KIDNEY (1492)
 SV40, DNA QUANTITATION, TRANSFORMED
 CELL (2373)
 SV40, DNA, RNA, CHINESE HAMSTER (1954)
 SV40, DNA, SUPERHELICAL, NICKEL (1951)
 SV40, DNA SYNTHESIS, ACTINOMYCIN D
 (0662)
 SV40, DNA SYNTHESIS, HAMSTER (1089)
 SV40, DNA SYNTHESIS, 3T3 (1952)
 SV40, ENHANCEMENT OF VIRAL TRANSFORMA-
 TION, UV IRRADIATION (0663)
 SV40, ENZYME ACTIVITY, SIMIAN KIDNEY
 CELLS (1506)
 SV40, FIBROBLASTS, LUNG (1490)
 SV40, GREEN MONKEY KIDNEY CELLS,
 RESISTANCE (0214)
 SV40, GROWTH, TRANSFORMATION, MOUSE
 CELLS (2370)
 SV40, HAMSTER CELLS, ANTIGEN (1525)
 SV40, HAMSTER LIVER TISSUE, HAMSTER
 FIBROSARCOMA, ARGINASE (1496)
 SV40, HERPES SIMPLEX, GROWTH IN TRANS-
 FORMED CELLS (1493)
 SV40, HUMAN, HAMSTER, KINETICS (0289)
 SV40, HUMAN ADENOVIRUS TYPE 16,
 SENDAI, IMMUNOSUPPRESSION, HAMSTER
 (1042)
 SV40, IMMUNIZATION DURING LATENCY,
 TUMORIGENESIS INHIBITION (0671)
 SV40, IMMUNOSENSITIVITY, HAMSTER (2449)
 SV40, INDUCTION, MITOMYCIN C, OTHER
 AGENTS (0660)

SV40, INDUCTION OF CELLULAR DNA SYNTHESIS (1499)

SV40, KIDNEY, STRUCTURAL PROTEINS (1953)

SV40, KIDNEY CELL, THYMIDINE KINASE, HAMSTER (0667)

SV40, KIDNEY CELLS, ANTIGEN (1538)

SV40, LENGTH OF VIRAL DNA MOLECULE, INFECTIVITY (1098)

SV40, LUNG, CHROMOSOMES, HAMSTER (1498)

SV40, MAMMALIAN RNA POLYMERASE, DNA (1103)

SV40, MITOMYCIN C, 5-BROMODEOXYRUIDINE MOUSE KIDNEY CELLS (0664)

SV40, MOLONEY, MOUSE OVA (1931)

SV40, MOUSE PERITONEAL MACROPHAGE, TRANSFORMATION (1096)

SV40, MYCOPLASMA, CHROMOSOME ABERRATIONS (0665)

SV40, PAGET'S DISEASE, X CHROMOSOME (0245)

SV40, PHYTOHEMAGGLUTININ, RAT LYMPH NODE CELLS, NONSPECIFIC ANTIBODY (1097)

SV40, PLAQUE FORMATION, INHIBITION, REPRESSOR, REVIEW (2157)

SV40, POLYOMA, CHROMOSOME MODALITY, REVERSION, MOUSE CELL LINE (0558)

SV40, POLYOMA, FIBROBLASTS, GLYCOLIPID (1102)

SV40, POLYOMA, GANGLIOSIDE ALTERATION (1091)

SV40, POLYOMA, MURINE SARCOMA, TRANSFER RNA METHYLASE (1950)

SV40, POLYPEPTIDE, PROTEIN (2369)

SV40, PROSTATIC CANCER, LACTATE DEHYDROGENASE ISOENZYMES, HUMAN, HAMSTER (1508)

SV40, PROSTATIC CARCINOMA, PROGESTOGEN TREATMENT (1505)

SV40, RAUSCHER LEUKEMIA, TRANSFORMATION, RAT (2376)

SV40, REPLICATION, VIRAL ANTISERUM, MONKEY KIDNEY (1495)

SV40, SUPERINFECTION, POLYOMA, MOUSE FIBROBLASTS (1092)

SV40, SURFACE AND TUMOR ANTIGENS, VIRUS-SPECIFIED DNA (0209)

SV40, SUSCEPTIBILITY, CHROMOSOME TRISOMY (2375)

SV40, TEMPERATURE-SENSITIVE REPLICATION, MUTANT (0666)

SV40, THERMOSENSITIVE SV40 MUTANT, DNA (1090)

SV40, 3T3 FIBROBLASTS, DENSITY INHIBITION OF CELL MOTILITY (1500)

SV40, TRANSFORMATION, RNA, DNA (2377)

SV40 TRANSFORMED, MOUSE CELL, SURFACE COMPONENT (0212)

SV40, TRANSPLANTATION ANTIGEN INDUCTION (0670)

SV40, TUMOR IMMUNITY, HAMSTER (1979)

SV40, UV-IRRADIATED, ANTIGENICITY (1537)

SV40, UV IRRADIATION, SURVIVAL (0668)

TRANSFORMATION, REVIEW (0390)*

SV40, VARIANTS, DNA TRANSFORMATION, HUMAN FIBROBLAST CELL (1095)

SV40, VIRAL DNA UPTAKE, DEAE DEXTRAN (1502)

SV40, X-RAY IRRADIATION, MICE (0211)

SV40 DEFECTIVE MALIGNANT TRANSFORMATION, HAMSTER CELLS (2372)

TEMPERATURE, POLYHEDRAL CYTOPLASMIC DEOXYRIBOVIRUS, REPLICATION (0189)

THYMECTOMY, TUMORIGENICITY, HAMSTER (1961)

TUMOR INDUCTION, CELL-FREE EXTRACT, NEUROBLASTOMA (0567)

TUMOR INDUCTION IN MAMMALS, FELINE FIBROSARCOMA (1872)

TUMORS, TUMOR ANTIGENICITY (0843)

TYPE A PARTICLES, INTRACISTERNAL, GERBIL FIBROMA (1869)

TYPE C, GLIOMA, HUMAN (1018)

TYPE C PARTICLE, EMBRYONIC CULTURE, RAUSCHER MURINE LEUKEMIA (0175)

VACCINA, HUMAN LYMPHOCYTES, CHROMOSOME ABERRATIONS (1879)

VACCINA, TRANSFORMATION, MOUSE EMBRYO CELLS (1415)

VIRAL ETIOLOGY, LEUKEMIA IN DOMESTIC ANIMALS, REVIEW (0389)*

VIRAL ETIOLOGY FOR "SPONTANEOUS" TRANSFORMATION, MOUSE EMBRYO FIBROBLAST CULTURE (1072)

VIRAL GENETIC MATERIAL, LETHAL MUTATION (0864)*

VIRAL REPLICATION, LATENT VIRUS (1733)

VIRUS-LIKE PARTICLES, GASTRIC AND LUNG CANCER, LEUKEMIA (1414)

VIRUS-LIKE PARTICLES, RHABDOMYOSARCOMA, EPIDERMODYSPLASIA VERRUCIFORMIS (1017)

VISNA, PROGRESSIVE PNEUMONIA, SLOW TRANSFORMATION (2297)

YABA, THYMIDINE KINASE, TUMORS (1429)

YABA TUMOR POX, ULTRASTRUCTURE (1430)

WOUND TUMOR, RNA TRANSCRIPTASE ACTIVITY (0148)

VITAMIN A

DEFICIENCY, SALIVARY GLAND NEOPLASM, 7,12-DIMETHYLBENZANTHRACENE, RAT (0308)

VITAMIN B12

3-METHYLCHOLANTHRENE, SKIN TUMOR, MOUSE (2234)

VITILIGO

ANEMIA, GASTRIC CARCINOMA (0777)

WALKER'S CARCINOMA

GASTRIC WALL, GROWTH, METASTASES, RAT (0763)

WART

ANTIGEN STUDIES, HUMAN (2017)

KERATIC PAPILLOMA, PAPILLOMA VIRUS, EPIDERMODYSPLASIA VERRUCIFORMIS (1516)*

WILM'S TUMOR

CLINICAL FEATURES, CHILDHOOD CANCER (1180)

HAMARTOMA, CONGENITAL ANIRIDIA (1709)*

NITRITE, 2-IMIDAZOLIDINE, RAT (2184)

PLASMA RENIN, HUMAN (2556)

WOOD DUST
ADENOCARCINOMA, NASAL SYSTEM (0113)
XANTHOGRANULOMA
JUVENILE, CYTOMEGALOVIRUS, VIRUS
(1518)*
YTTERBIUM
DOSIMETRY, MEDULLARY CANAL, FEMUR,
RAT (1405)*

GADOLINIUM, CARCINOGENESIS (0403)
ZINC
DEFICIENCY, INHIBITION OF TUMOR
GROWTH, WALKER 256 CARCINOSARCOMA
(1232)
SKIN NEOPLASIA, LEUKOCYTE ZINC CONTENT
(0787)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

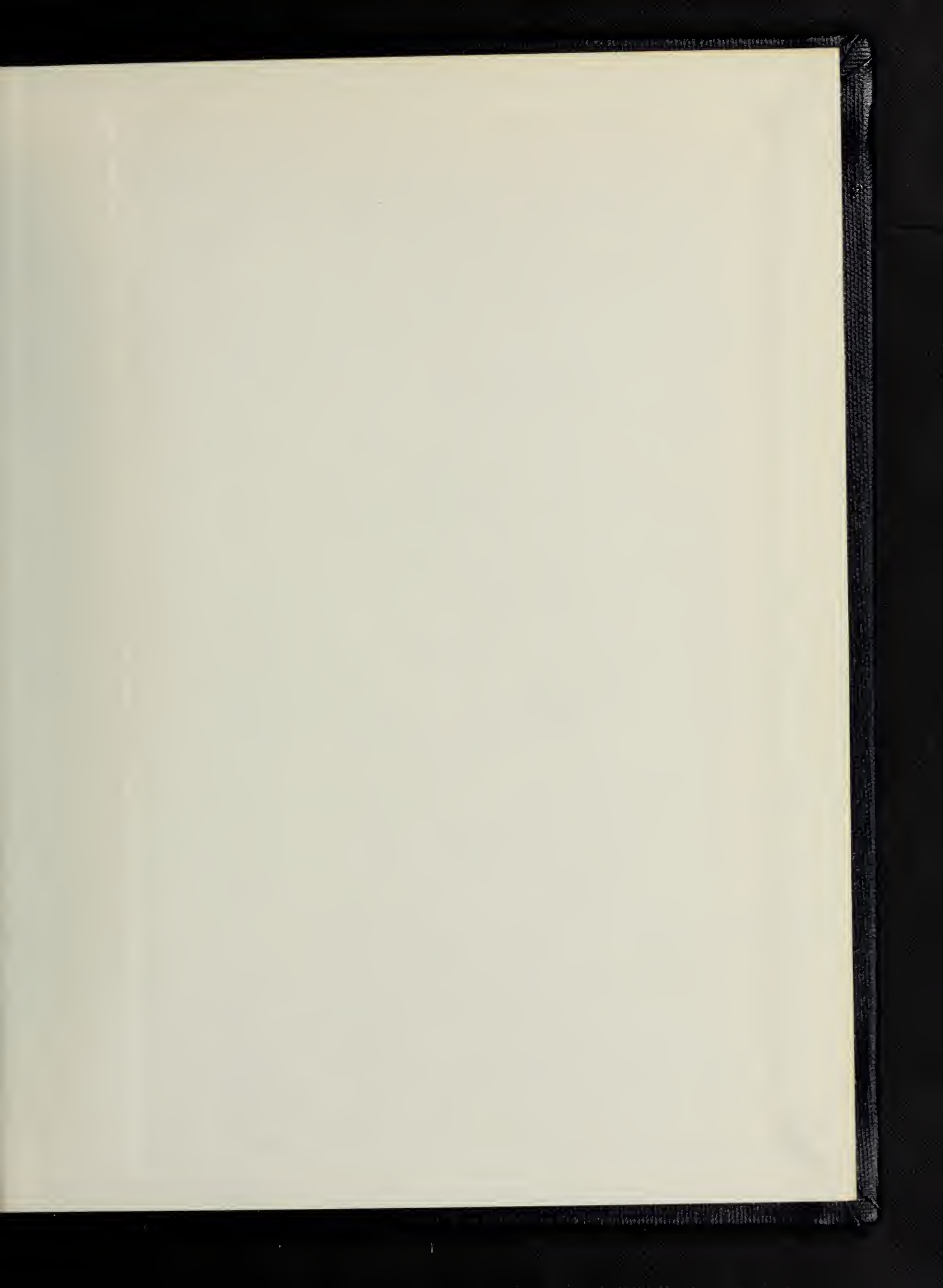
OFFICIAL BUSINESS

PENALTY FOR PRIVATE USE, \$300

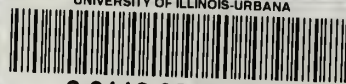
If you do not desire to continue receiving this publication, please CHECK HERE ☐;
tear off this label and return it to the above address. Your name will then be
promptly removed from the appropriate mailing list.







UNIVERSITY OF ILLINOIS-URBANA



3 0112 084231718